UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF TEXAS
TEXARKANA DIVISION

COPY

THE STATE OF TEXAS	*	CIVIL NO.: 96-CV-0091
	*	
VS.	*	JUDGE: DAVID FOLSOM
	*	MAGISTRATE:
THE AMERICAN TOBACCO COMPANY, Ft AL	*	JUDGE WENDELL C. RADFORD
	*	JURY TRIAL DEMANDED

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Charleston, SC

VIDEOTAPED DEPOSITION OF

JAMES T. WILLERSON, M.D.

VIDEOTAPED DEPOSITION AND ANSWERS of James T. Willerson, M.D., taken before Teresa Saucier, a Certified Shorthand Reporter and Notary Public in Harris County for the State of Texas, in the law offices of Williams Bailey Law Firm, L.L.P., 8441 Gulf Freeway, Suite 600, Houston, Harris County, Texas, on the 7th day of September, 1997, between the hours of 11:52 a.m. and 6:18 p.m., pursuant to Notice, the Federal Rules of Civil Procedure, signature of the witness being requested.

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P R O C E E D I N G S

(Willerson Exhibit No. 1 was marked for identification by the reporter and is attached hereto.)

THE VIDEOGRAPHER: It's Sunday, September the 7th, 1997. The approximate time is 11:52 a.m. We're on the record.

JAMES T. WILLERSON, M.D.

was called as a witness, and being first duly cautioned and sworn by the court reporter to testify to the truth and nothing but the truth, thereupon, in answer to questions propounded by counsel, testified as follows:

EXAMINATION

BY MR. CORNFELD:

Q. Would you state your name, please, sir?

A. I'm Dr. James T. Willerson.

Q. Doctor, what is your occupation?

A. I am a physician and cardiologist.

Q. All right, sir. And your business address?

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A. I have two. One is at the University of Texas Medical School at Houston and the other is at the Texas Heart Institute, St. Luke's Episcopal Hospital, Houston.

Q. You understand that we are here for your deposition in the State of Texas's lawsuit against various tobacco companies?

A. I do.

Q. And that you have been designated as an expert witness --

A. I do.

Q. -- for the State of Texas --

A. I do.

Q. -- in that case?

All right. And we just met before the deposition began, but let me introduce myself again. I'm Rick Cornfeld. I'm here to take your deposition on behalf of the Defendants in the case, as I'm sure you understand. Have you had your deposition taken before?

A. About this issue?

Q. About any issue in any case.

A. I have been deposed before. Actually, a very few times and I think probably the last time was certainly more than five years ago. It might

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have been more than ten years ago.

Q. All right.

A. This is not something I do with any frequency.

Q. I guess not. I don't know if you recall the -- the procedure, but I'm sure it's been explained to you. I'll be asking you questions. If at any time you don't understand one of my questions or maybe you don't even hear one of my questions, would you let me know so that --

A. I shall.

Q. -- I can rephrase it?

And if I use a term incorrectly within your field of expertise, will you let me know that also?

A. I shall.

Q. Okay. Dr. Willerson, what is your -- your position at the University of Texas Medical School in Houston?

A. I'm a professor of medicine and the chairman of the department of internal medicine.

Q. All right. And your position at the Texas Heart Institute?

A. I'm the medical director and chief of cardiology.

Q. All right. Before the deposition sometime ago, a copy of your curriculum vitae was provided to

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us. Let me hand it to you. It's now been marked as Exhibit 1 to the deposition. It bears the date on the top, April 9, 1997, so perhaps it's not totally up to date. Would you -- would you take a look at it and let me know whether this is your current curriculum vitae and whether it is accurate and, if not, what -- in what respect it's not accurate or up to date?

A. Well, it changes a little bit every month generally, so there are a few manuscripts that you don't have that are actually in press or might have even been published, but -- and maybe a few other things that would be entered in some of the other categories like honors or textbooks, that kind of thing, but shy of that, it is mine and it's approximately up to date.

Q. Is there anything significant that's not on the -- on Exhibit 1?

A. Maybe to me, not to you.

Q. Actually, I meant in terms of this lawsuit.

A. No.

Q. Okay. Is there anything not -- that's not on Exhibit 1 that relates to tobacco in any way?

A. Repeat the question.

Q. Is there anything that's not on Exhibit 1 that

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relates to tobacco in any way?

A. That would be new?

Q. Yes, sir.

A. No.

Q. All right. You've -- you've said there are some honors that -- that aren't on Exhibit 1. Can you tell me about those?

A. I've been selected to give a distinguished lecture at the upcoming meetings of the American Heart Association in November. One person is selected annually to give this lecture and for me, it's an honor.

Q. When will that be?

A. In November, mid-November.

Q. Where will the lecture be?

A. In Orlando, Florida.

Q. And what will be the topic of your lecture?

A. I'm going to talk about the detection of unstable atherosclerotic plaques and gene therapy for the protection of unstable atherosclerotic lesions. If I go too fast, you tell me, please.

Q. Actually, it's the -- the court reporter who should tell you.

A. All right.

Q. If you do go too fast for me, I'll let you know

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too.

A. All right. I've also been made aware that I'm going to be the honored guest of the Houston Chapter of the Texas branch of the American Heart Association. I'm their medical honoree for this year and there will be a dinner given in my -- in my name.

Q. That's at Orlando? That -- that dinner will be given --

A. No, no, no. That's here in Houston.

Q. Oh, I see.

A. In February. That's a separate honor to me.

Q. Oh, I see. That's a -- that's a dinner that the Houston branch of the American Heart Association is going to hold?

A. In my honor.

Q. I see.

A. There may be one or two other things that I -- there are one or two other things that I know about that I think will be announced shortly, but I don't believe they're really relevant to -- to this.

Q. All right. Do any of them involve giving a lecture or writing a paper?

A. No. I don't believe so.

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Q. All right. You said the paper -- excuse me, the lecture you're going to give at the American Heart Association is going to relate to the detection of unstable atherosclerotic plaques for gene therapy?

A. It's the detection of unstable atherosclerotic plaques at risk to abruptly transition themselves so they cause heart attacks or strokes.

Q. All right.

A. And some data that we have about how one might protect such plaques using various forms of gene therapy.

Q. I see.

A. So, it is complicated.

Q. Does that have anything to do with whether the cause of the patient's condition for which you are proposing to use gene therapy has a genetic basis?

A. Well, I think in -- the strong -- one of the strongest risk factors for the development of atherosclerosis is the genetic risk. That's one of the very strongest risks. But what I'm going to talk about is trying to identify those patients who are at risk to abruptly develop heart attacks or strokes. What this involves is

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we have shown that there is temperature heterogeneity in so-called vulnerable atherosclerotic plaques, the same plaque as in different segments of it, differences in temperature. The hotter portions of the plaque correlate with areas of inflammation. We've been able to detect these in a variety of ways, but the one most applicable to humans by infrared imaging. And this should be one of the first means of detecting a vulnerable atherosclerotic plaque. Of all of us in the room, it would be likely that each one of us would have at least one atherosclerotic plaque. Hopefully, none of them are vulnerable, none of them are abruptly susceptible to ulceration or fissuring that might lead to a heart attack or a stroke. But these methods that we've developed and insights that we have who are very helpful are going to be predictive of this so that, ultimately, one might know not only about the presence of atherosclerosis, but who really has very vulnerable lesions. And then we have developed some gene therapy methods at least in animal models are protected. Whether they'll be in humans, I don't know, but we'll be finding that

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out in the near future.

Q. What you've just described, is that true for everybody or is it true only for patients whose condition has a genetic basis?

A. I don't know about everybody. We haven't studied everybody.

Q. All right. But, I mean, is it true for people other than just those who have a genetic basis for their disease?

A. Again, you're asking for a very wide survey and we haven't conducted a wide survey. Our analyses are in more than 200 patients with atherosclerotic plaques and a very large number of animals, but 200 patients is not the total population at risk. So, you know, among those 200 patients do I know that every one of them had a genetic risk for atherosclerosis? No, I don't.

Q. Did you -- did you determine in those 200 patients what had caused their disease?

A. That's not possible to do in many people. Some have genetic risks. Their parents had heart attacks or strokes at an early age, so they, by definition, have a genetic risk. Others have high cholesterols or LDLs. Others smoke. Others have high blood pressure or diabetes and some of

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them have combination of those things. And those are well-established risk factors for atherosclerosis.

Q. In fact, many people have combinations of risk factors who --

A. Some do.

Q. -- don't --

A. Some do.

Q. Would -- would you say it's -- most people that develop heart disease have a combination of risk factors?

A. I would say some do.

Q. Have you ever looked to see what percentage?

A. I'd have to know the total denominator in the world with atherosclerosis to tell you a percentage.

Q. Are you aware of --

A. I don't know the total denominator.

Q. Are you aware of any studies that have looked to see --

A. No one has a total denominator.

Q. Well, let me finish my question.

A. I'm sorry.

Q. Studies that have looked in a particular population to see what percentage of people in

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that population had their disease because of a combination of those factors?

A. With all due respect to you, let me point out something that would be evident, and that would be in any population, no one would know the total number of individuals or arteries with atherosclerosis. At the moment, that takes an invasive study to determine it. In some instances, one could detect the disease at a localized organ like the heart with a non-invasive study, but one would have to screen every member of that population to know the denominator. Then we could talk about a percentage with disease. Then we could talk about a percentage of those with a certain risk factor or combinations. There's no question that a certain number of people have multiple risk factors. There's no doubt about that. But I see patients who seem to have predominantly one or two risk factors. Every cardiologist does. And I see some who have multiple risk factors. I'd rather see those with only one or two risk factors that are easier to help.

Q. Because you can get rid of just that one or maybe two risk factors?

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A. If you can control the one or two -- we don't have a good way to control the -- that genetic risk usually yet. But if you can control one or two other nongenetic risk factors, then one expects to attenuate the development of atherosclerosis, slow its progression anyway.

Q. Are you aware of studies -- I appreciate the explanation you gave me, Doctor, so let me ask it this way: Studies that have looked at populations with known atherosclerosis? I understand that there may be people who have atherosclerosis, but there's no way to know, but studies of populations with known atherosclerosis --

A. No.

Q. -- to determine whether they have multiple risk factors to a greater extent than people who have just one risk factor?

A. Almost every culture with any sophistication in medicine has tried to examine a certain number of individuals within that culture from various socioeconomic strata that have atherosclerosis and they try to determine why they might have atherosclerosis and what can be done about it and intervene in various ways seeing if they can

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change the prognosis of individuals. But there's still a very serious limiting factor for those studies if we're going to talk about percentages that have this, that or the other; and, that is, it's a subset of the total. And I don't believe anyone can accurately give you a percentage unless you know the total denominator. I know what you would like for me to try to do and, that is, estimate how many people with atherosclerosis have a single risk factor versus multiple ones. It's very hard to do for the reasons that I've mentioned. There are people who fall into both categories, as best one can tell. I'm afraid that's the best I'm going to be able to do for you.

Q. What you're saying is some people would fall into one category, some people would fall into another category, but you would have no way of determining how many fall within one or the other or even estimating the number?

A. Without knowing the total denominator, it would be hard to know.

Q. And you don't know the total denominator?

A. No one in the world does.

Q. All right. So, not only with -- without knowing

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the total denominator would it be hard to know, but as I understand what you're saying, without knowing the total denominator, you couldn't and you don't believe anyone else could, with any reasonable accuracy, estimate the number of people with single risk factors or a combination of risk factors; is that right?

A. I think precise estimation would not be possible. That doesn't preclude identifying risk factors or getting some personal assessment on the basis of experience of a physician or data that are published -- both hopefully -- what might be the most important risk factors. I certainly have very strong opinions about that that I'll be happy to share with you if you ask me.

Q. Can you determine, with any reasonable degree of certainty, how -- how many or what portion of people with atherosclerosis have any particular risk factor?

A. We have a limitation that I've mentioned, and you understand it and I think everybody who's listening or will see this would. That's the inability to know the total denominator.

Q. All right.

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A. What was your question again?
Q. I'm just trying -- I'm just trying to be thorough about this. I think --
A. I -- I know, and I'm trying to be careful in what I say.
Q. Yeah. I -- I understand. I -- I need to ask the question even if I have an idea of what the answer is going to be.
A. Repeat it again. I just want to be sure I've again protected myself. Go ahead.

MR. CORNFELD: Would you read it back, please?

THE WITNESS: He can't remember either.

MR. CORNFELD: Well, I want to make sure I get it exactly right.

(The question was read by the reporter.)

A. Have some risk factor.

COURT REPORTER: "Any particular."

Q. (BY MR. CORNFELD) Have any particular risk factor.
A. Okay. So, that would be some risk factor, one or more risk factor. This would be based on people

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that I see. I would say to you that of the people that I see, which is not the total group, that I can find a risk factor, at least one, in the majority of them.

Q. In what percentage of people can you find no risk factor?

A. A minority.

Q. How big a minority?

A. Very small minority that I see.

Q. All right. Doctor, can you tell me what you understand your role to be in this lawsuit?

A. To answer questions within my area of expertise about the impact of smoking on cardiovascular disease.

Q. What do you understand this lawsuit is about?

A. I'm going to have to answer that in sort of an awkward way, and it would be that I'm a doctor. I'm just a poor doctor taking care of people. And I've been asked to share my experience and expertise in caring for patients with cardiovascular disease, which is now more than 30 years of effort in this area, as it relates to the risk from tobacco use for cardiovascular disease. I'm not an expert on all the details of this lawsuit. I haven't read about it widely. I

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haven't tried to find out details about it. I was asked to render my expertise in this area and I gladly do that.

Q. Do you have any idea what the State is claiming in this case, what they're trying to recover?

A. Again, as I just said, I have not made any attempt to learn that kind of information.

Q. Does that mean you're -- you're not aware of what --

A. That would mean that I'm not completely aware of it for sure.

Q. Well, tell me what you -- what you understand.

A. I'm going to try to say it one more time. I have not looked into these details at all. If you ask, you know, you might -- maybe you can satisfy yourself by asking me specific questions. I'm under oath --

Q. That's what -- that's what I'm trying --

A. -- about whether I know certain facts about the lawsuit. I think you're going to find that I know very little about it, if anything.

Q. Doctor, that's what I'm doing. I'm -- I'm trying to ask you. I understand you have not looked into this in any detail, but what I would -- what I would like to know is whatever you have looked

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at it or heard about it, what do you understand this case is about? What is the State claiming and what are they trying to recover?

A. I -- I do not know what they're trying to recover and I do not know the full extent -- extent of their claims.

Q. Beyond that this -- that this case involves in some way an issue or issues about the impact of smoking and cardiovascular disease, do you have any understanding of what the case involves?

A. That is the extent of my knowledge.

Q. All right. How did you become involved in this case?

A. I was asked to become involved by some of the lawyers for the State of Texas.

Q. Who is that?

A. Well, there are two in the room (indicating). The gentleman to my right and the lady on the end to my left.

Q. What is the name of the lady at the end? I have not met her.

A. Well, we might let her tell you her name. Her name is Harriett.

MS. CHANEY: Chaney.

MR. MONTGOMERY: It's Dr. Harriett

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Chaney. She's with the Williams Bailey law firm.

Q. (BY MR. CORNFELD) Okay.

A. They're not friends of mine or close colleagues of mine or confidants of mine. They simply asked me to be involved.

Q. And the other individual is -- is Mr. Montgomery?

A. Yes.

Q. All right. When did they ask you to become involved?

A. I don't remember the precise date, but it's a very few months ago, maybe -- maybe two months ago or -- two to three months ago, something like that. Might be a little longer. It's within the past year. It's within the last eight months and I think about three months ago.

Q. All right. Tell me the -- the first contact you had.

A. I believe it was a phone call from one or the other and -- asking me if I could be available to share my medical experiences and expertise as it relates to cardiovascular disease and the impact of smoking on cardiovascular disease. I said that I would make myself available. Subsequently, there was an initial visit in my

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office.

THE WITNESS: Harriett, you came and I think you came -- you came with someone else, didn't you? Who did you come with?

MR. MONTGOMERY: They won't let us answer questions.

THE WITNESS: They won't let you answer.

MR. MONTGOMERY: You just give your best recollection that you have.

A. (Continuing) She -- she came with another lawyer. I don't remember the name.

Q. (BY MR. CORNFELD) All right.

A. And they talked to me about, again, whether I would be willing to share my expertise. And they asked me a few questions about how long I had been in cardiovascular medicine, what my positions were, what I knew about the physiologic impact of tobacco use on the cardiovascular system, medical questions, what the evidence for my opinions would be, where was there such written support. I made them aware of a textbook that I'm the author of, probably several textbooks, and, in general, some publications in the cardiovascular literature over the last

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several years. They thanked me for being willing to share my expertise, said they would like to enlist my help. I pledged my help. Subsequently, I -- you know, this is all from memory. It's my best recollection of it. I believe the next contact was to make me aware of a date when my deposition would be taken. It was to be a Saturday, a week ago, I think, one to two weeks ago last week, I think. And at the last minute, that proved to be inconvenient to me because of several very ill patients. And so we tried to change it to an evening, I think maybe a Sunday evening. That was not acceptable to the lawyers that would be involved. It was rescheduled for today. We held one other meeting, the two lawyers whose names you do have and myself, which was on the day my testimony was supposed to be given. They came to my office and I found a few minutes for us to talk. And we reviewed -- they had copied some of the articles that I made them aware of in portions of my book. We looked at that, talked a little bit about what would be expected of me in this deposition. That was probably about a 30 or 40-minute visit and they left. I think that's my

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sole contact with the lawyers for the State of Texas.

Q. All right. The initial phone call -- strike that.

If I understand, just to sum up, the contacts you've had have been one initial phone call, a subsequent meeting with Harriett Chaney and Kendall Montgomery?

A. No. It was not with Kendall.

Q. No. I'm sorry.

A. It was with another lawyer whose name I'm embarrassed to say I don't remember. But you can find that out easily enough --

Q. All right.

A. -- from Harriett Chaney. Go ahead.

Q. Okay.

A. That part is right.

Q. All right. And then -- and then a second meeting which was when your deposition was originally scheduled?

A. Right. Not at precisely that time, but on that same day.

Q. All right. And that's -- and that's the entire extent of the contact you have had?

A. It's quite possible that there's another phone

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call or two wherein -- in trying to adjust these meeting times and trying to determine why I couldn't be present at the time of the original deposition. I know there was another phone call or two. My secretary was involved and maybe exclusively involved, although I think I talked to Harriett too to apologize for not being able to be present at the deposition as originally scheduled and trying to explain why. My secretary told me she was concerned that I couldn't make that first date. I suggested an alternative one, as I mentioned, in the evening and then she called back to say that would not be acceptable and we agreed on this one. So, there's one or two other phone calls, but they're about practical issues relating to meeting time.

Q. Okay. The -- those two meetings and the one phone call, are they the only contacts you have had related to either the issues in this case or the substance of your opinions?

A. Apart from the ones that I mentioned to try to find the right time to meet, to the best of my recollection, they are the only ones.

Q. Those phone calls you had regarding scheduling and the one where you -- where you apologized for

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having to change the original date of the deposition, did you discuss the substance of your testimony or your opinions or the issues in this case?

A. If I did, I would have had to have been asked some questions by them. That's not a subject that I would have raised. And I don't -- I don't remember in the subsequent phone calls any discussion of the case, per se, only whether I would be there or not and the need to devote six hours, which was a problem when it was first scheduled.

Q. All right. The -- doctor, the initial phone call that you -- that you had, how long did that last?

A. It was brief. My secretary told me that lawyers representing the State of Texas were trying to reach me to determine whether I would be willing to share my expertise in this area of inquiry. And I asked my secretary to call the lawyers back and allow me to tell them that I would. And that probably took five minutes, maybe less.

Q. All right. Did the individual who called you on that occasion ask you any of your opinions regarding any area within your expertise?

A. I don't -- you know, this goes back several

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months ago, so you're really testing my memory.

Q. I understand.

A. But I -- I don't think so, not in the phone call, but then there was a meeting which I've described in which two lawyers came to my office and we did discuss my experience as a cardiologist, my insights as regards the impact of smoking, tobacco use on cardiovascular disease, how my insights were formed, as I mentioned, what the evidence for my insights might be. That was done. And I provided that information.

Q. Okay. I -- I understand. I was -- I was asking about the -- the phone call, but let me ask --

A. I don't believe in that phone call there was any real attempt to find out what my expertise was. They seemed to know a little about me already --

Q. All right. Did -- did they --

A. -- in that phone call.

Q. Did the individual or individuals who telephoned you inform you any -- about what this lawsuit was about?

A. Not in detail, no.

Q. Do you recall what -- anything they said?

A. Only that their -- that the State of Texas had a lawsuit against the tobacco industry and it

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related to the impact of tobacco use, smoking, on cardiovascular disease, and that's really the full extent of what I know about the lawsuit.

Q. All right. In the meeting that you held, the -- the first of the two meetings, how long did that last?

A. Again, it's awhile ago, but it was not a long meeting for sure. I don't hold too many long meetings.

Q. I'm -- I'm getting that idea.

A. But about 30 minutes, probably about 30 minutes.

Q. Did the lawyers provide you with any information or materials?

A. About the lawsuit?

Q. Or about anything.

A. I don't remember their providing me with anything.

Q. Have the lawyers --

A. I think they gave me their business cards. They did provide me with that.

Q. All right. Other than their business cards, have the lawyers in this case or anyone else on behalf of the State of Texas, ever provided you with anything?

A. No, sir, not to the best of my memory.

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Q. All right. Now, you've -- you said -- strike that.

Have you read any depositions in this case?

A. No, sir.

Q. Have you been told about any depositions in this case?

A. Minimal. At -- at the meeting that I held with the two lawyers about a week ago, they made me aware that Dr. Charles Lemaistre had been deposed. They know that Dr. Lemaistre is a friend of mine. He's the president of -- former president of the M.D. Anderson Cancer Center and a friend of mine. And they told me a little bit about his deposition; one, that it had been long and arduous; two, that it had been a bit challenging and confrontational; three, that they hoped mine wouldn't be the same; four, they advised me to stick to my area of expertise, to try to make it not confrontational and arduous. I believe that's the sum and substance of what I learned about any single deposition.

Q. You don't know the identity of any other witnesses in this case?

A. I was told on the way over here today that a doctor in Dallas whom I also know is an expert

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witness for the tobacco industry in the same area in which I'm an expert witness for the State of Texas.

Q. Who is that?

A. His name is Dr. Grammer in Dallas. But I don't know the substance of his deposition. I don't even know if it's been taken yet.

Q. You said you were informed of that on the way over here?

A. Uh-huh.

Q. By whom?

A. By the lawyer on my right.

Q. Mr. Montgomery?

A. Yes.

Q. Did -- did he drive you here?

A. Yes.

Q. So, that's a -- I guess not a formal meeting, but at least it's another contact you have had?

A. It certainly wasn't a formal meeting. It took us about ten minutes to drive over here. I didn't know how to get here and I asked them, the lawyers, if they would provide the transportation, transportation for me. They picked me up at my -- at the hospital. I was seeing patients. They were trying to make it

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easy for me to get here and they're going to take me back at the end of the -- this certainly was not any formal meeting.

Q. Okay.

A. This was idle discussion on the way here.

Q. I -- I got to tell you if somebody had picked me up, I might have made it here on time.

A. Well, I -- I was worried I wouldn't, so that was the way to come. They might have picked you up too. We might have all ridden together if you had asked.

Q. If I would have even known who to ask. Well, Doctor, if we can get back to that -- well, strike that.

Let me -- let me ask about Dr. Lemaistre. Were you informed what his opinions were that he gave in his deposition?

A. In the discussion that made me aware that he had given his deposition, I think I was informed of at least one, and that was that he was asked whether he thought tobacco use led to lung cancer. And I was told that he stated adamantly that he did.

Q. Were you told --

A. And that's the -- that's the only one that really

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sticks in my mind. I know that to be the case. That's not any surprise to me. I know his feelings about that. We've discussed them before. He and I have a close professional relationship and work closely together in the Texas Medical Center. So, I'm fully aware of what he would say to most questions like that. But I think that was the only point. If there was something else that was discussed, I don't remember it.

Q. Were you told in what way that that deposition was confrontational?

A. No.

Q. Whether he had any trouble answering any questions?

A. No.

Q. All right. Now, Dr. Grammer, you said you know him?

A. I do.

Q. How do you know him?

A. Well, I was in Dallas for 18 years. I was -- from the period of 1972 to 1989, I was in Dallas at the University of Texas Southwestern Medical School and Parkland Memorial Hospital. I was the chief of cardiology there for the last ten years

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of that period. Dr. Grammer worked -- I think he still does -- at a hospital right across the street from Southwestern and Parkland Hospital, St. Paul's Hospital, where he is a cardiologist. And so he and I would occasionally interact over a patient. At one point, I was trying to extend our training program from Parkland to the St. Paul Hospital. And, occasionally, I would see a patient of Dr. Grammer's for a second or third opinion. I would see him socially occasionally at a party.

Q. Do you have respect for Dr. Grammer as a cardiologist?

A. Yes.

Q. Is -- is Dr. Grammer -- do you have respect for his honesty and integrity?

A. Do these questions really relate to my own sharing of my expertise in the area of tobacco use and cardiovascular disease?

Q. Well, if -- let me -- let me put it this way, Doctor: If you're going to come in at trial and in any way criticize Dr. Grammer's expertise or his honesty or -- or anything other than simply disagree or perhaps agree with various things that he has testified to, that's something I'm

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entitled to know about.

A. All right. Well, let me answer it this way: I hope it would suffice. I have no intention of coming into a trial and criticizing anyone. I would come and share my expertise about tobacco and cardiovascular disease. I'm not coming to -- to disgrace anyone.

Q. Doctors can disagree on -- on issues --

A. Of course.

Q. -- and still have respect for each other; is that right?

A. Yes, of course.

Q. Same -- same as with lawyers --

A. Right.

Q. -- and people in any other profession?

A. Of course.

Q. And the mere fact that you might -- strike that.

Do you have any -- any idea of the substance of Dr. Grammer's testimony in this case?

A. Not really.

Q. Did you ever discuss tobacco with Dr. Grammer?

A. No, sir.

Q. Did you ever discuss other risk factors for heart disease with Dr. Grammer?

A. I'm smiling because I've been out -- away from

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Dallas for eight years. My interaction with Dr. Grammer was very sporadic and relatively infrequent. It was not on a frequent basis. And so you're asking me to remember whether I've ever discussed a risk factor with him. Around the care of a patient, that's what it would have to be. I don't recall any discussion with him.

Q. All right. If you can then return to the -- actually, to the conversation you had on the way over here -- because I want to try and get that off the table if it should be off the table -- did you discuss in the conversation you had with the attorneys on the way to the deposition --

A. With the attorney.

Q. Attorney?

A. With the attorney.

Q. Okay. Mr. Montgomery. Did you discuss the substance of this case or any of the opinions that you hold?

A. No.

Q. Okay. All right. Then the -- then the -- the meeting that you had in your office which was the first meeting that you had in this case, you said you discussed at that meeting in approximately 30 minutes the physiological impact of smoking, the

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evidence you have to support your opinion on the physiological impact of smoking, and you referred to various textbooks and publications that were --

A. Generally to the cardiovascular literature, yes.

Q. All right. Did you discuss anything else?

A. Nothing of substance that I remember.

Q. All right.

A. Do you have a specific question about that?

Q. I -- I will.

A. Okay.

Q. In fact --

A. You better ask it.

Q. -- I probably whatever we have left of the six hours of specific questions about it, but my --

A. It would be better if you ask me a specific question about it because that might jog my memory about something. In the meeting that I had with them --

Q. Yes.

A. -- I do not remember anything else of substance other than what I've shared with you. If you have something you want to ask me about, please do so because I want to be completely candid with you --

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Q. Okay.
A. -- the best that I can.
Q. The -- is it -- is it the case, Doctor, that you understand that the opinions you have that are related to this case and that you intend to provide at the trial of this case relate to these issues of the physiological impact of smoking on the cardiovascular system and the evidence to support that impact?
A. The physiological, the biological, the medical, the prognostic impact of smoking and tobacco use on cardiovascular disease. That is what I am prepared to discuss primarily. I don't mean to exclude something that might be relevant to this for which I have not mentioned an appropriate phrase, but, in general, that's the area that I -- that I am prepared to discuss.
Q. All right. What did you tell the attorneys at the -- at that initial 30-minute meeting regarding the -- without using any modifiers, let's just say regarding the impact of smoking on the cardiovascular system?
A. Define "modifiers" for me.
Q. Physiological, biological. I -- I don't want to get caught up in whether something's

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physiological or biological. I'd really just like to know what you said about the impact of smoking.

A. Well, I think smoking is a major risk factor for cardiovascular disease. I don't believe there's any doubt in the world about that. The evidence is overwhelming for that statement and my own personal experience in the care of patients. And in certainly experimental studies that have been -- that I've been part of having -- of overseeing, that the evidence that some component of smoking or components causes alterations physiologically that lead to cardiovascular disease is quite clear. And I stressed that to the lawyers. I did go on to point out in some specific terms what some of the physiologic and biochemical, biologic medical alterations are that occur in individuals and experimental animals that smoke which are adverse to the cardiovascular system. And I emphasized that as a cardiologist who sees very large numbers of patients with heart disease that I think smoking is one of the very major risk factors for heart attacks and progressive atherosclerosis. That's not word for word what I said to them, but it's

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in general what I said.

Q. Did you -- did you explain what you believe are the alterations in the cardiovascular --

A. Yes, I did.

Q. -- system that you believe result from smoking?

A. I did.

Q. What are they?

A. You want to know the physiology and --

Q. Yes.

A. -- biology of that?

Q. Yeah. I -- I assume what you're going to tell me is what you told the attorneys at that meeting.

A. The best -- the best I can remember --

Q. Your opinion hasn't changed on this since that day?

A. My opinion has not changed since that day.

Q. All right.

A. Smoking injures the inner lining of the arteries, the vascular endothelium. It allows the insudation of lipids into the artery. It promotes blood clot development by exerting an effect on platelets causing them to aggregate. It is a vasoconstrictor of the artery. This is probably related to its injury to the endothelium. And these actions then can lead to

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the narrowing of an artery and the development of a blood clot in the artery. There's also substantial evidence to show that smoking affects serum lipids adversely by reducing high-density lipoprotein or HDL concentrations. This is true of both frank smoking and passive smoking. That also would lead to risk of heart attacks since that lipid is a protective one and one that removes cholesterol from plaques. There's also some effect on low-density lipoprotein and very low-density lipoprotein to increase both of them. And these are adverse effects as well on the process of atherosclerosis since they contribute directly to atherogenesis. And I believe that smoking causes a fibroproliferative change as well that's imminently linked to its impact on thrombosis. All of these effects are very disadvantageous to one who -- who uses cigarettes and who either has or is destined to acquire atherosclerosis. There are a couple of other physiologic points. Smoking increases heart rate that causes a heart to need more oxygen, and in a heart where the arteries are already narrow, that's a disadvantageous effect. And it increases blood pressure, smoking

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increases blood pressure at least acutely, and that may also require more oxygen by the heart and is similarly disadvantageous. And I think that I should mention one other thing and, that is, smoking may lead to lung disease, may lead to emphysema. And patients who have emphysema have a lowered oxygen tension in their blood. And the heart depends on a certain oxygen tension. And when that's lowered, that has a very disadvantageous effect on the function of the heart. These are some of the things that I told them and I think most of them.

Q. All right. There was some things in the beginning of your answer that I didn't -- I didn't quite catch, so I wonder if the court reporter can read back the answer up until the point where I'm sure I did get it and then I'll stop you.

(The requested testimony was read by the reporter.)

Q. (BY MR. CORNFELD) Doctor, these are the -- are the various ways in which you believe smoking exerts its effect on the cardiovascular system?

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A. These are at least some of the ways that smoking exerts its effect on the cardiovascular system.

Q. Is there anything else?

A. Well, that probably remains for additional research to show.

Q. Oh, all right. These are the ways that are --

A. These are the known ways --

Q. All right.

A. -- that smoking exerts its effects on the cardiovascular system.

Q. All right, sir. And this is what you explained to the attorneys in the initial 30-minute meeting --

A. I did.

Q. -- you had. All right. And then you said -- well, strike that.

Did you -- did you tell them anything else about the impact of smoking on the cardiovascular system; in other words, what that impact is?

A. This is most of what we discussed. I don't remember sharing additional information with them about this.

Q. All right. Now, you said you also discussed the evidence to support this impact. Let me go through and ask you about that. The -- what you

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said about smoking injures the inner lining of the arteries and that is -- that lining is called the vascular endothelium?

A. Uh-huh.

Q. Is that right?

A. Uh-huh.

Q. You need to say "yes" or "no" for the court reporter.

A. Yes. I'm sorry.

Q. Okay.

A. Yes.

Q. And then you said that smoking allows the insudation of the lipids into the arteries. Is that the mechanism by which smoking injures the inner lining?

A. The smoking itself or some constituent of smoking injures the endothelium and that injury is a physiologic injury that causes the artery to constrict as we discussed a minute ago. But that injury is also associated with allowing the retention or insudation of lipid in the artery. So, it's a physiologic effect that smoking has on the vascular endothelium that leads to the entrapment of lipid and also the -- the attraction of the platelets which are the nidus

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for the blood clot development and then the vasoconstriction.

Q. But the platelets are the what for the blood clot development?

A. The platelets are the nidus, the nidus. They are the initial substance that -- that leads to the formation of blood clots. Platelets are formed blood elements. They circulate in our circulations. When the vascular endothelium is injured, platelets adhere to that site of injury, then aggregate, build up, and that's the initial scaffolding for the blood clot development. Those platelets are joined by white blood cells and red blood cells in a match and that's the substance of the blood clot or thrombus as we refer to it medically.

Q. All right. Incidentally, did the attorneys either at this meeting or any other meeting tell you when and where the trial of this case would be?

A. I believe that was mentioned at this meeting. It's been mentioned subsequently. I asked about that on the way over here today and I know -- I know where it is and I know approximately when it is.

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Q. All right. It's in Texarkana?
A. Yes.
Q. And it will be sometime this fall?
A. In late September is what I believe.
Q. Right. And did you indicate that you were available to travel to Texarkana to testify?
A. I don't seem to have much choice about that.
Q. All right. So, that's a "yes"?
A. Yes.
Q. All right. The -- the injury to the vascular endothelium, do I understand that there are three aspects to that, the allow -- allowing of the insudation of the lipids, the effect on platelets and the vasal constriction?
A. Those are consequences of the injury to the endothelium.
Q. What does word "insudation" mean?
A. Entrapment, retention.
Q. What is it that smoking does to the inner lining or to the vascular endothelium that leads to these three effects?
A. Well, I used the word "injures" and I think that's probably the most accurate way to describe it because one can show post-smoking in experimental animal models and in humans a

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vasoconstriction that did not exist previously in those arteries in response to the administration of certain substances. I don't know how much detail you want about this, but --

Q. Go ahead.

A. -- there -- there is a substance called acetylcholine which is used to test the normalcy of the vascular endothelium. This substance is delivered directly into an artery, humans or animal models, and one expects the artery to relax in response to it. When the endothelium is injured, it is referred to as a dysfunctional endothelium. The artery constricts rather than relaxing. Acetylcholine is an endothelium-dependent vasodilator and when the endothelium is injured, it has a paradoxical effect to constrict the artery. This is one of the substances, not the only one, but one used to test the normalcy of the endothelium physiologically. After smoking, one can demonstrate a vasoconstrictor response in response to acetylcholine. One can also demonstrate a smaller lumen, a reduction in the luminal diameter after smoking acutely and chronically. One can demonstrate the aggregation of platelets after smoking in humans or

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experimental animal models, and this has been done in several ways, but one is to take a blood sample from the individual before and after smoking and show that smoking promotes the aggregation of platelets in a test tube to a much greater extent to substances that are agonists for platelet aggregation, promoters of platelet aggregation. And there are experimental studies that have been done to show the retention of lipid in arteries that have been exposed to smoking.

Q. All right. Doctor, by the phrase "aggregation of platelets," do you mean something more -- well, strike that.

What do you mean by aggregation of platelets?

A. Clumping of the platelets.

Q. So -- so, if you would draw blood from an individual after that individual has smoked and you look at the platelets in the blood, you will see that they are clumped together?

A. No. What you can -- you -- you might -- in some circumstances, you might see that, but the way this -- what you expect to find is if you then separate the platelets from that blood sample and you test their clumping capability -- there are

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standard methods for doing this -- you can show that they clump much more avidly, much more severely, in response to substances that cause them to clump ordinarily, but that effect is markedly promoted in the circulation that is seen, the constituents of tobacco and smoking.

Q. All right. Doctor, what are the studies that show that smoking injures the vascular endothelium? Right now, I'm asking not about the studies that show that there is insudation of lipids or aggregation of platelets or vasoconstriction because you said those are the effects of the injuries, but the studies that show the injury to the vascular endothelium.

A. Well, I believe that you've been given that information. I didn't come with a list of them today, but I believe that you have a summary of the information related to that both in my own textbook, Cardiovascular Medicine, in some journal articles from Circulation and other journals that have been made available to you and certainly you could find it yourself if you made any attempt to --

Q. Well --

A. -- look into the cardiovascular literature over

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the last two or three years. But I believe that you or your colleagues have been given that information.

Q. Well, Doctor, I'm asking you now to tell me what they are. I -- I know I can go to the library and try to find almost anything, but you're the expert in the case.

A. And my -- and I'm telling you that you have that information.

Q. Well, which ones are they? We were -- we've been provided a whole lot of things. And I'm not a doctor and certainly the jury's not going to be doctors. You're not going to just say, "Here, jury. The studies are in" -- "are in this group." What I'm asking you is can you tell me which studies those are that show that?

MR. MONTGOMERY: Well, do you want him to go through? We can hand him the stack.

Q. (BY MR. CORNFELD) Mr. Montgomery has a stack of studies in front of him. Are the studies you're talking about in there? I don't believe those have been provided to us before. But, Doctor, are they in there?

A. I'm going to have to look for a minute. I don't

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know without looking.

Q. All right.

A. How would I know?

Q. Okay.

A. May I ask them a couple of questions? Am I permitted to do that? Because I don't know whether they copied everything that I mentioned to them. I don't have any way of knowing that.

Q. Well, let -- let me ask you: What -- what is it that you're looking for?

A. At the -- well, I'm looking to see if in general the things that I mentioned to them are in this stack.

Q. Do you have any particular studies in mind that you're looking for?

A. There's a host of studies and it includes work summarized by Drs. Glantz and Parmley, G-l-a-n-t-z, and Parmley.

THE WITNESS: Harriett, are they in this stack?

Q. (BY MR. CORNFELD) Are they in that stack, Doctor?

A. I'm about a third of the way through it, so if you want me to answer that accurately, you're going to have to give me a minute. And I

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mentioned others, work by Kannel and Castelli, a summary of risks of smoking in a chapter in my book by John Oates, O-a-t-e-s, of "Risks of Cardiovascular Disease" written by several authors in my book. It's all in a section entitled "Cardiovascular Risks."

THE WITNESS: Does he have a copy of my book, Cardiovascular Medicine? Can we ask that he buy one? Does the law firm buy one?

A. (Continuing) That would simplify your look. The reviews by Parmley and Glantz are going to have most of the information, most of the information that you'll find relevant. And several of those are in circulation and I haven't found one of those here yet, but -- but they tell me that they copied them. And then also work by Winniford, W-i-n-n-i-f-o-r-d, and Hillis, H-i-l-l-i-s, which has been published in the last seven years, eight years.

THE WITNESS: Was that copied, Harriett, too? Is it in -- is it in this stack? Is everything that I asked you to copy in this stack? I don't see some of it is what's slowing me down a little. Is

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there some that's not in this stack? Do you know?

MR. MONTGOMERY: I'm not sure anyone knows the answer.

THE WITNESS: Okay.

MR. MONTGOMERY: You'd just have to review. Is that the book chapter --

THE WITNESS: Yeah.

MR. MONTGOMERY: -- you're talking about?

THE WITNESS: This is a summary from the book.

A. (Continuing) I don't see several of those manuscripts here including some of the work by Parmley and Glantz and Winniford and Hillis about smoking. Also, work by John Folts, F-o-l-t-s, on the influence of smoking on thrombus development. I don't know whether the chapter by Oates is copied from my own book. But those are some of the specific references that you're asking me about. Now, how do we get him to -- to a chapter by -- Oates is here on smoking.

Q. (BY MR. CORNFELD) And that's in -- in which book?

A. My book, Cardiovascular Medicine.

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Q. All right.

THE WITNESS: How do we get to him copies of these things or is he expected --

A. Are you expected to find this after I tell you the references?

Q. (BY MR. CORNFELD) If you -- if you can give me the -- I have a feeling we're not going to finish today, so if you can provide the citations to Mr. Montgomery following the conclusion today and he can provide them to me before we -- I'll have them before we resume again.

Doctor, you -- you --

A. Let's just stay with it for a minute, okay?

Q. Okay.

A. I'm going to circle some things here that I want to make you aware of. Would that be a way to help you?

Q. That would be fabulous.

A. Good.

I should mention too that -- strong evidence that there is some reduction in risk of cardiovascular disease including heart attacks in men and women who stop smoking for certain periods of time, especially those who have never smoked heavily. I've circled some of those

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references in what I've just given you.

Q. Okay.

A. You're going to want to hold that out because I've turned down pages and circled some.

Q. Doctor, let me pre -- preface what I'm going to say by saying this: To my mind, talking about evidence of either increases or decreases in heart attacks is not exactly what we're talking about here. What we're talking about here are the physiological effect of smoking to injure the vascular endothelium.

A. Right.

Q. Okay. And I will certainly get to evidence of effects in populations who have either had an increase or a decrease in heart disease or maybe no change.

A. Okay. Mr. Cornfeld, with all due respect to you, I think that the proximate cause of heart attacks is a development of a blood clot which is the consequence of injury to the endothelium, and I think information about reductions in risk of heart attacks after smoking cessation or associations of increased risk of heart attack associated with smoking are directly relevant to what I am discussing with you.

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Q. Okay.

A. And you have put me on a search through these manuscripts of some support for the statements that I've mentioned. And I'm deep at work on the task which you have assigned me and am turning down pages for you. I think I may -- I may feel that I've been a consultant to you by the time this is over.

Q. That's -- that's what taking a deposition is all about, Doctor.

A. These papers by Glantz and Parmley are not in here and I hope we can get somebody to look at Circulation, the last couple of years.

MR. MONTGOMERY: Okay. Well, you've mentioned them to him. They're documents that they can find also. We've provided -- everything that was actually pulled and given to you is here today. So, there may have been things you mentioned that didn't get pulled.

A. (Continuing) I won't take too much more time in doing this. I -- give me just a minute more.

Q. (BY MR. CORNFELD) Sure.

A. I can give you some of this right now. It will be very helpful.

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Q. Whatever -- whatever you want to take, Doctor.
A. I should also make it clear that I -- my comments so far in our interaction have emphasized coronary heart disease alterations, but peripheral arteries suffer the same impact as coronary arteries in atherosclerosis. And occlusive events involving peripheral arteries occur just as they do in coronary arteries for the same reasons.
Q. Okay. Well, I'll -- thank you, Doctor. I -- I certainly will not neglect that.

Have you completed your review of the literature?

A. Well, not quite.
Q. Okay.
A. This paper by Auerbach and Hammond is an autopsy study and -- with macroscopic and microscopic assessment bracketed in there -- would be of interest to you about development of atherosclerosis in smokers, which is subsetted with endothelial injury. Well, without taking a really long time, I think the things if -- if we have to provide this information, if I have to provide this information that would be useful are articles by Glantz and Parmley and Winniford and

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Hillis would be very helpful in their -- some recent papers in Circulation on passive smoking too and its effect on lipids in children and adults.

Q. Those are in addition to what you have provided to me just now?

A. Yes.

Q. All right.

A. But they are not in addition to what I had mentioned earlier to the lawyers who asked me.

Q. I -- I understand. And --

A. It's not in this stack.

(Willerson Exhibit No. 2 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) All right. Specifically, Doctor, you have handed me what I have now marked as Willerson Exhibit 2, which is an excerpt from the book you edited, Cardiovascular Medicine. And specifically, you turned back -- since this won't show up on all the photocopies that are ever made, I'll specify. You turned back pages 1833 and 1834 and you circled references 7,

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Kannel, et al., 1984; 8, No. 8, Rosenberg, 1985; No. 9, Rosenberg, 1990; and No. 13, FitzGerald, 1988; is that right?

A. But, please, let me --

Q. Excuse me first. Is that correct?

A. That -- I did do just what you said, yes.

Q. All right. And why -- why did you circle those references?

A. Because I think they're relevant to information that you seem interested in acquiring related to the impact of smoking on cardiovascular disease and the physiologic, biologic, medical impacts of smoking on cardiovascular disease.

Q. All right, sir.

A. But that was not meant to be limiting in any way. That section of Cardiovascular Medicine from our book contains other information as well and that's why it's made available to you. It's just that in the few minutes you've given me -- or you've given me all the time I want, but in the few minutes I feel comfortable in taking in looking through it quickly, those are areas that I thought would be of particular interest relevant to answering your question or request of me.

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Q. All right, sir.
A. This whole pack of information, these reprints generally has information relevant to what you've asked me to provide. And as I've identified, there are some manuscripts, some work done by others that's not in this stack --
Q. Did you provide --
A. -- that you'll have to get.
Q. Did you provide that work done by others that is not in this stack that you brought to the deposition? Did you provide those to the attorneys for the State of Texas?
A. I did not provide anything to them directly. I simply mentioned references and works that I'm familiar with that would be supportive of my concerns about tobacco use and smoking and their impact on cardiovascular disease. I didn't provide anything directly. I provided general references.
Q. Did you give them the citations?
A. Specific citations, no. Authors and general location of these citations, yes.
Q. All right. Let me continue with the -- with the papers that you just handed to me that you've indicated provide support for your opinion about

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smoking's effect on the vascular endothelium.

(Willerson Exhibit No. 3 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) Exhibit 3 is a paper from JAMA of April 5, 1995 by Glantz and Parmley; is that right?

A. Finding the title page is the problem with the author's name on it.

Q. I'm sorry. I should have handed that to you with that sheet on top.

A. This is by Glantz and Parmley. It's copied upside down.

Q. Actually, I think it's just stapled upside down.

A. Probably. But it is by Glantz and Parmley and this is one of the articles that I was interested in. It's in JAMA.

Q. All right. Is this the work by Glantz and Parmley that you had reference to --

A. Well, it's --

Q. -- a few minutes ago?

A. It's some of the work. It's not all of the work. It's some of the work. It's some of the

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review of a body of work not done just by Glantz and Parmley, but done by many physician scientists in the past several years.

Q. All right. You -- you've indicated that -- in an earlier answer when I asked you what studies show the injury to the vascular endothelium that there was a host of studies that were summarized by Glantz and Parmley. Is this the summary that you're talking about?

A. It is -- it is one of the summaries. It's not the only one.

Q. Glantz and Parmley have done other summaries that you have in --

A. Yes.

Q. -- mind?

A. Yes.

Q. All right. Where are those summaries?

A. Well, that's what we just talked about a minute ago. And I -- if it is obligation -- I -- I don't know how one does these matters, but -- but I had mentioned to the -- some of the lawyers for the State of Texas who talked to me that some of that work is in the journal Circulation over the last two or three years and some of it's in other places. It's not limited to that. So, we have

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an article here from the Journal of the American Medical Association or JAMA. Some's in Circulation and you're going to find some in other places too.

Q. Do you rely on that other work by Glantz and Parmley for any of your opinions in this case?

A. My opinions are really personal ones established as a result of my own experience in caring for patients with cardiovascular disease over more than 30 years. They are the result of my oversight of certain experimental studies that have been done in patients exposed to smoking, tobacco use in laboratories for which I was responsible. And they are the result of many things that I have reviewed, many articles that I have reviewed, read, such as ones by Parmley, Glantz, but others, too in my role as the editor of Circulation, which is the Heart Assoc -- American Heart Association's largest journal. And I've been the editor of it since 1993 as well as my general experience in cardiovascular medicine, of more than 30 years attending meetings, listening to papers, reading papers, being critical about work, serving as a reviewer of manuscripts that are submitted. It is the sum

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of all of that.

Q. Doctor, is the work that Glantz and Parmley have done that is in places other than Exhibit 3 --

A. The JAMA article.

Q. Yes -- among the materials that you rely upon for your opinion regarding smoking's effect on the vascular endothelium?

A. Okay. You just asked me that question, Mr. Cornfeld, with all due respect.

Q. I'm -- I'm not sure I got an answer to that. What I --

A. Well, yes, sir, you did.

Q. You -- you said that you rely on -- on all kinds of materials for all of the things you know about cardiology. At least that's how I understood your answer.

A. That and --

Q. So --

A. Excuse me.

Q. So, that's why I would like an answer specifically to this question regarding the work by Glantz and Parmley other than Exhibit 3. Do you rely upon that work for -- at least, in part, for your opinion regarding smoking's effect on the vascular endothelium?

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A. May I repeat in part what I said before?
Q. If it answers that question, go ahead.
A. I believe that it does. I tried before and I now try again. My opinions about the impact of smoking on cardiovascular disease are the sum, the totality, of my own personal involvement in the care of patients with cardiovascular disease over more than 30 years, the result of my oversight of certain experimental studies done largely in humans in which tobacco and smoking was used to try to establish its impact on cardiovascular responses, and all that I read, all that I review and all that I hear over a period of more than 30 years, including while I've been the editor of Circulation. Now, that does include, but is not limited to, the work of Glantz and Parmley.
Q. All right. I -- I didn't mean to suggest that it was limited to anything.

Doctor, with respect to Exhibit 3, you folded down one page of that exhibit for me. Unfortunately, the number -- the page number does not appear on this photocopy, but you also checked the sections in that -- on that page that are headed "Platelets" and "Atherosclerosis"; is

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that right?

A. Yes, sir, I did.

Q. Why did you do that?

A. In my quick look at the material that's here, I was trying to find some areas of relevance in some of these manuscripts that have been copied that would be useful to you in addressing the question that you asked me to provide specific support for my opinions that smoking injures the endothelium, promotes thrombosis, vaso-constriction, atherosclerosis and fibroproliferation. So, as I look through these articles, this one included, the JAMA article by Glantz and Parmley, in a quick look, I found these areas which I thought would be very helpful to you in answering the question. That help is not limited -- in this article is not limited to these sections, but I think does include these sections. And I thought you wanted something relatively quick to refer to and I wanted you to have it.

(Willerson Exhibit No. 4 was marked for identification by the reporter and is attached hereto.)

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Q. (BY MR. CORNFELD) All right. Doctor, then another paper that you handed me has now been marked Willerson Exhibit No. 4. That's a paper in the Journal of Cardiac Rehabilitation by Kannel, et al., in 1984 entitled "Latest Perspectives on Cigarette Smoking and Cardiovascular Disease: The Framingham Study," and in particular, you folded back the first page of that paper and marked the abstract for me; is that correct?

A. Yes, sir, I did, and for precisely the same reasons as I --

Q. All right.

A. -- marked the other paper in a certain spot.

Q. Is this the paper by Kannel and Castelli that you mentioned to me earlier when I asked you what are the studies that show injury to the --

A. It is --

Q. -- vascular endothelium?

A. It is one of them. It is one of them.

Q. When I -- when I mentioned that to you -- excuse me. When I asked you that question earlier, I have in my notes that you referred to a study by Kannel and Castelli and I think you referred to one study. Is this -- I -- I know Kannel and

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Castelli have done a lot of work for decades on smoking and on cardiovascular disease. All I want to know now is: Is this the study that you meant in your earlier answer?

A. Please let me answer it the way I just did. It is one of them. The -- the -- if you -- if you would allow me just to continue a little further. This Framingham evaluation has been very important in American epidemiological evaluations because it took a group of patients in Framingham, Massachusetts and followed them for a period of time trying to establish risk factors for the development of cardiovascular disease and other diseases too, but primarily cardiovascular disease. Castelli and Kannel -- and Kannel, actually, have been leaders of that kind of evaluation, as you already know, for -- for many years. So, there have been numerous papers that have come from that work. This is one of those papers. This is one that I thought would be helpful in supporting the positions that I've expressed, but it's only one of several. It's not the one or the only one. It's one of several.

Q. All right. Why is it that this paper is in front

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of us and not any of their others?

A. Well, I -- I didn't -- I didn't personally copy these papers. I mentioned, as I've said I think a few times now, that I made some of the lawyers for the State of Texas aware of some of the work that would be very useful in identifying risks of cardiovascular disease in patients that smoke. I didn't try to make them available all of the work. That might take the rest of my career to do that. I tried to make them aware of some of the work. This is some of the work and it's not even all of the work that I mentioned to them.

MR. MONTGOMERY: Rick, let me add something before you go on with your question. Just so that you understand so there's not a misconception, he gave his opinions and these are papers that were pulled simply from him listing a list off of the top of his head much like he's done here in the deposition and were not a series of papers he asked to review in order to form opinions. They were just off-the-head references.

A. (Continuing) This was very spontaneous.

MR. MONTGOMERY: Those that got

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written down kind of like you've had trouble writing down as he talks are what copies have been made of.

Q. (BY MR. CORNFELD) Doctor, did you look at the stack of papers that's in front of us today prior to this --

A. No, sir --

Q. -- morning?

A. -- I did not.

Q. Prior to the beginning of the deposition, did you do so?

A. No.

Q. So, there was a --

A. I -- in fact, I -- no, I did not.

Q. Have you looked at any stack of papers or collection of papers in connection with this case?

A. Yes, I have. I was sent a group of papers that were among those that I had mentioned by the lawyers in the mail and asked whether these were some of those that I had mentioned in our early meeting. And I made them aware that they -- these were some of those that I had mentioned. I didn't bring them with me today. I did leaf through them actually earlier today and they're

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not exactly the same as these. Some of them are probably the same, but there's some in that group that are not here, I think.

MR. MONTGOMERY: That would be the group that you've got.

MR. CORNFELD: All right. I -- my understanding is that the witness was to bring with him all of the materials on which he was relying.

A. (Continuing) I wasn't asked to do that, Mr. Cornfeld.

Q. (BY MR. CORNFELD) You were not asked to?

A. No, sir.

Q. You were not asked to bring anything?

A. I was not asked to bring anything.

Q. All right.

MR. MONTGOMERY: And pursuant to what are you saying he should be bringing anything?

MR. CORNFELD: Pursuant to my understanding of an agreement among the -- among the attorneys, pursuant to which we stopped serving document requests in connection with the depositions.

MR. MONTGOMERY: No. Everything that

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had been provided to him in advance had already been sent to you, and these were more of the type of references that he was mentioning where he simply threw things off the top of his head, so we brought those. But you have everything that he's --

MR. CORNFELD: Okay.

MR. MONTGOMERY: -- made reference to or has.

(Willerson Exhibit No. 5 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) Doctor, the -- the last paper that you handed me that you went through -- that you took out when you went through your stack of papers was --

A. When I went through the lawyer's stack of papers.

Q. The ones that were in front of you?

A. Right.

Q. And that's now been marked as Willerson Exhibit 5. That is a paper in CHEST that is by Auerbach, et al., 1976 entitled "Cigarette Smoking and Coronary Artery Disease"?

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A. Yes, sir.
Q. All right. Is that -- and you also folded back the first page along with the -- the abstract which you marked?
A. I did.
Q. All right.
A. For exactly the same reasons as I marked the others --
Q. I'm sure.
A. -- in the same places that I've expressed to you.
Q. Okay. Let's identify the other papers that are -- that were brought.

(Willerson Exhibit No. 6 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) Dr. Willerson, is Exhibit 6 a paper from Circulation, 1993, by Sugiishi and Takatsu entitled "Cigarette Smoking is a Major Risk Factor for Coronary Spasm"?
A. Let me -- yes, it is. And I would like to say to you that some cardiologists use "spasm" as "vasoconstriction," which is the word I used, in describing the physiologic effects of smoking on

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vascular endothelium. They use them synonymously, spasm meaning obliteration of a luminal artery, vasoconstriction meaning a narrowing of it and they're often used synonymously. They, in fact, are not exactly synonymous and I prefer the term "vasoconstriction," but this certainly would be a paper that would be supportive of my statement that there is a vasoconstriction or, if you want, spasm associated with cigarette smoking.

Q. All right.

A. Yes. And it is from Circulation, January, 1993, and it is by Drs. Sugiishi and Takatsu.

(Willerson Exhibit No. 7 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) All right. Is Exhibit 7 a paper by McGinnis and Foege entitled "Actual Causes of Death in the United States" from JAMA in 1993?

A. Yes, sir, it is.

(Willerson Exhibit No. 8 was marked

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for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) Exhibit 8, is that a paper from a journal I'm not going to attempt to pronounce. It looks like it's from Scandinavia.

A. Scandinavica, I think.

Q. Well, there's another word. That, I could have handled. It was the word in the middle there that --

A. Okay. Chirurgica.

Q. Okay.

A. All right. Yes, sir, it is. November/December 1988 issue.

Q. All right. And what is the -- what is that paper?

A. "Cigarette Smoking and the Outcome After Lower Limb Arterial Surgery."

Q. By whom?

A. Lassila and Lepantalo.

Q. All right.

(Willerson Exhibit No. 9 was marked for identification by the reporter and is attached hereto.)

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Q. (BY MR. CORNFELD) Deposition Exhibit 9 is a paper from Circulation by Schlant, S-c-h-l-a-n-t, et al., "The Natural History of Coronary Heart Disease," published in 1982; is that right?

A. Yes, that's right.

MR. CORNFELD: I think I'm out of stickers.

(Willerson Exhibit No. 10 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) Defendant's Exhibit 10 to this deposition is a paper from Circulation by Willerson, et al., from 1989 entitled "Specific Platelet Mediators and Unstable Coronary Artery Lesions"?

A. Yes.

Q. All right.

(Willerson Exhibit No. 11 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) Exhibit 11 is a paper from the

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American Heart Journal in 1982 by Nobuyoshi, et al., entitled "Statistical analysis of clinical risk factors for coronary artery spasm: Identification of the most important determinant"?

A. Yes.

(Willerson Exhibit No. 12 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) Exhibit 12 is from the Journal of Cardiopulmonary Rehabilitation by Miller, et al., entitled "Position Paper of the American Association of Cardiovascular and Pulmonary Rehabilitation. The Efficacy of Risk Factor Intervention and Psychosocial Aspects of Cardiac Rehabilitation"?

A. Yes.

(Willerson Exhibit No. 13 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) Exhibit 13 is from the

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American Heart Journal, 1992 by Nobuyoshi, et al., entitled "Statistical analysis of clinical risk factors for coronary artery spasm: Identification of the most important determinant"?

A. Yes.

Q. And that -- that's actually a -- just a duplicate of Exhibit 11; is that right?

A. It appears to be.

Q. All right.

(Willerson Exhibit No. 14 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) Exhibit 14 is from the Journal of Cardiac Rehabilitation and I think this is another duplicate. This is -- looks to me like a duplicate of the Kannel paper that you identified earlier; is that right?

A. I'll have to look back to be sure it's a duplicate of the --

Q. Sure.

A. -- one we just looked at.

Q. Sure. Let me hand you Exhibit 4.

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A. Yes. They're the same.

(Willerson Exhibit No. 15 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) All right. And Exhibit 15 is a copy of a paper from the British Heart Journal in 1983 entitled "Cessation of smoking after myocardial infarction, Effects on mortality after 10 years" by Aberg, A-b-e-r-g, et al.; is that right?

A. Yes, sir, it is.

(Willerson Exhibit No. 16 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) Finally, Doctor, the last item that was -- that was in the stack of materials that the State's attorneys brought to the deposition has now been marked as Willerson Exhibit 16. Can you tell me what that is?

A. I didn't prepare this list, so I'm not sure.

Q. Do you have any idea what that is?

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A. I probably can guess. Is that what you want me to do?

Q. Your guess is probably better than mine, so go ahead.

A. I didn't bring the page here and it was not shown to me in advance, but it certainly looks like some of the manuscripts or portions of them that were -- may have been copied and are listed in summary as being useful in the evaluation of smoking and tobacco and their impact on cardiovascular disease.

Q. All right. Let's -- let -- let's see. For example, there's a reference in Exhibit 16 to that Scandinavian journal which is Exhibit -- and we have a Scandinavian journal that's Exhibit 8. Does the reference on Exhibit 16 correspond to Exhibit 8?

A. This is useful in some way in my answering this?

Q. I -- I hope so. We'll find out.

A. It's useful and relevant, both?

Q. We'll find out. Those are your two questions you get to ask me during the course of this deposition, Doctor.

A. I think I've already asked a few others. Well, maybe the way to answer whether this is relevant

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is to try to find that page number and this article, and I think you asked me about the Scandinavian --

Q. Yes.

A. -- manuscript. So, what's listed here, is it page -- for that journal what's listed on this sheet are pages 1180 and 1174 are the two listed and those pages are not included in this particular article. So, I think it's something different.

Q. All right. But you have no idea what --

A. I didn't make the list; I didn't see the list earlier. I'm only guessing at what it represents.

MR. CORNFELD: How much time do we have on the tape?

THE VIDEOGRAPHER: About seven minutes.

Q. (BY MR. CORNFELD) Okay. Doctor, you mentioned to me earlier work by Winniford and Hillis?

A. Right.

Q. Can you tell me about that work?

A. These were studies that were done in a cardiac catheterization laboratory at Parkland Hospital in Dallas while I was the chief of cardiology at

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that institution. So, they were done in the time period between 1984, '85 and '89. And they evaluated the influence of smoking on cardiovascular responses in humans and demonstrated that smoking acutely in nonsmokers previously and in those who smoke increased heart rate, increased blood pressure, led to coronary artery vasoconstriction. Those were the primary findings in those studies.

Q. During what years was -- were those studies done?

A. It was in that range of time that I just mentioned to you, and, you know, remembering the precise year is going to be a little difficult for me to do, but in the time period between -- I said 1984 and 1989. Probably we ought to have a broader perspective because it wasn't just one study. It was several studies.

Q. All right.

A. And it was done, I think, in the time period -- it was a series of ongoing investigations and it was -- I'll give you a broad range, Mr. Cornfeld. And it was in the period of 1975 to 1989. And they are published in the New England Journal of Medicine and in several other places, I think including Circulation, but

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I'm not positive about that. But it is a series of studies establishing the points that I just mentioned.

Q. You were at Parkland from '75 to '89; is that right?

A. In fact, I was at Parkland from 1972 to 1989.

Q. Okay.

A. I was certainly there during the time period 1975 to '89.

Q. Was that work going on by Winniford and Hillis prior to your arrival at Parkland?

A. No. It's work that I encouraged.

Q. All right. Would you spell Winniford and Hillis?

A. It is Dr. Michael Winniford, W-i-n-n-i-f-o-r-d, and Dr. L. "D" as in "David," Hillis, H-i-l-l-i-s.

Q. All right. Is this the work that you meant when you said that there was work that was done under your supervision --

A. Yes, sir.

Q. -- in your laboratory?

A. In our laboratories. Yes, it is.

Q. Is there any other such work that you had in mind?

A. Primarily this -- these studies in humans

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directly under my supervision.

Q. Do any of those papers appear on your curriculum vitae?

A. I don't think so. I was not a coauthor in them. I was responsible for encouraging that work to be done and suggesting that it be done trying to establish in an objective way the influence of smoking on cardiovascular responses.

Q. Is -- was there any animal studies that were done in your laboratory or under your direction with regard to this issue?

A. No.

Q. So, when you -- when you told me that there was -- that -- that part of what you rely on for your opinion regarding the effect of smoking is work that was done in your laboratory, what you had in mind was the work by Winniford and Hillis?

A. In humans exposed to tobacco and smoking, yes.

Q. All right.

A. Part of what I had in mind was that.

Q. But that's all of what you had in mind when you said there was work that went on in your laboratory on the effect of smoking on humans; is that right?

A. That was part of what I had in mind and that did

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address the -- the issue of work that went on in our laboratories, yes. That was the work that went on in our laboratories.

Q. And there's no other?

A. You know, you're again testing my memory over a 25-year time period. You're asking me to say that there was no other.

Q. That's all you can recall?

A. And I'm a little reluctant to say that.

Q. Okay.

A. And you would be too in the same position. That's -- this was the primary work. That's for sure.

Q. All right. I -- I don't have anything else -- if you're -- if you're thinking that I've got some other paper by some -- some other doctor and I'm going to say, "Aha, you didn't tell me about it" --

A. No.

Q. -- I just want -- I just want to make sure I know everything.

A. I wouldn't believe you would do that, Mr. Cornfeld.

Q. I would never do that because I'm not smart enough.

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A. But I -- but -- but I -- I want to answer you honestly.

Q. Okay.

A. And that's why I struggle with some of these answers, particularly when they relate to a 25-year time period and every single thing that we did. I -- it's hard to be absolutely certain about always, never, only, those -- that's tough.

Q. Okay. All right.

A. But this is what I primarily had in mind about this aspect of work done in our laboratories.

Q. All right. Doctor, the -- you also mentioned to me work by John Folts. How do you spell Folts?

A. F-o-l-t-s.

Q. F-o-l-t-s. Where is that work?

A. Well, first of all, Folts is in Wisconsin and the work emanates from there and his work is in several places as well. You know, I know more about the work than remembering exactly the precise place something was published. I wonder whether anyone could --

Q. I'm not --

A. -- over a 30-year time period.

Q. No. That wasn't --

A. But -- but I think -- I -- I think that it's in

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Circulation.

Q. Okay. Can you tell me about that work?

A. Yes. It was work done in experimental animal models and it was done in dogs primarily, but probably -- possibly not limited to dogs. These were dogs that had an injury to the endothelium, a mechanical injury to the vascular endothelium, that were then exposed to smoking and a demonstration that the smoking caused thrombus development at the sites of vascular injury in these dogs. And I believe that Folts tried to identify some protective interventions that would then prevent the smoking-induced thrombus development, blood clot development, in these animal models. I think he did, tried to find a protective intervention. And he may have found that aspirin provided some protection. I'm not as sure about that, but certainly the impact of smoking on thrombus development, he was one of the investigators who -- who showed that in a relevant indeepo (sic) model.

Q. You said this work occurred over a 30-year period?

A. No. I -- I said -- you asked me --

Q. Oh.

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A. I was trying to --
Q. Okay.
A. -- remind you --
Q. I understand.
A. -- that you were asking me to remember precise citations during the 30 years that I've been involved in cardiovascular investigation and work and I've said that's hard to do.
Q. How long --
A. I remember work better than I remember precisely where it was published.
Q. All right. And -- and maybe you are not going to remember precisely when the work was done, but if you can give me an idea over what period of time.
A. I believe -- I believe it was done in the late 1970s. Folts' work was done in the late 1970s, probably the period between 1976 and -- late 1970s, early 1980s, the ten-year period between 1976 and 1986.
Q. Doctor, in -- in this case, did you do a literature search or -- in terms of the literature that you told the State's attorneys about and the literature that you told me about and I assume the literature under which you

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intend to rely in the testimony at trial, have you and are you relying on your recollection of that work?

A. I did not do a literature search. I was not asked to do a literature search. I was asked to provide my opinion and to provide some substantiation of that opinion in terms of investigators' names and generally where the work might be just as I've tried to do for you and am trying to do for you. I did no literature search and I am not planning to do a literature search.

Q. Okay.

MR. CORNFELD: Are we finished with the tape? Why don't we take a break, then.

THE VIDEOGRAPHER: The time is 1:48 p.m. We're going off the record.

(Short recess.)

(During the break, Mr. Montgomery left the deposition proceedings.)

THE VIDEOGRAPHER: The time is approximately 2:15 p.m. We're on the record.

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Q. (BY MR. CORNFELD) Doctor, when did you come to believe that smoking had an effect on the vascular endothelium?

A. I don't know a precise moment or even a year, but certainly at this point after a rather extensive involvement in caring for patients and all the things you've heard about, I do have that very strong conviction that smoking is very injurious to the vasculature in a variety of ways, including injury of the endothelium. It's something that's developed in me over a period of years of caring for patients and being involved in cardiovascular medicine in the ways you know I'm involved.

Q. Well, you -- you completed medical school in --

A. 1965.

Q. All right. Were you aware of it then?

A. No, not -- certainly not to the extent I am today. I probably -- if someone had asked me if I thought it were injurious, I probably would have said "It might be," but this is a conviction that has developed in me after a long period of involvement in cardiovascular disease. In graduation from medical school, of course, I wasn't a trained cardiologist.

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Q. All right.

A. I was very much a generalist. So -- this is relevant. I spent from 1965 to 1972 becoming more specialized in medicine after graduating from medical school. I was intern and resident and spent almost three years in training in cardiology, two years at the National Institutes of Health and working in a research lab and actually began my career as a cardiologist in 1972 after that training. So, when I talk about 25 to -- years, I'm talking about that period from '72 on. In fact, it's longer than that. It's almost 30 years.

Q. If you count from when you started your -- your post-medical school training?

A. Right.

Q. All right. Well, when you were a research and clinical fellow in the cardiac unit and department of medicine at Massachusetts General Hospital from '69 to '72, were you aware of smoking's effect on the cardiovascular system?

A. I was certainly becoming aware of it during that time.

Q. At that time, did you believe that smoking had an injurious effect on the cardiovascular system?

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A. You're smiling because we're again going way back in time for a thought that I had. It is a conviction that I have developed from that time until now increasingly stronger, every year stronger conviction over some period of time. I believe if you had asked me in 1969 to 1972 "Do you think that smoking injures the cardiovascular system," my answer probably would have been similar to what I would have said right after medical school, "probably, possibly," but the conviction has developed over the more recent years with a lot more experience.

Q. Now, is -- does -- is the general medical community -- do you -- do you believe is the general medical community convinced that smoking has an adverse effect on the cardiovascular system?

A. I believe that the knowledgeable medical community very strongly believes that smoking has an adverse effect on the cardiovascular system.

Q. Is that accepted within the field of cardiology?

A. Yes, sir.

Q. For how long has that been accepted within the field of cardiology?

A. Several years. I can't tell you how many, but

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several years. Some -- some period of time. That's not a recent revelation, but some period of time.

Q. Was that the case when you were a resident?

A. You know, we would have to distinguish between what the leading authorities in cardiovascular medicine knew when I was a resident and what I knew that they knew. I wasn't one of them at that time. I think I am today, honestly, and I can answer your question today, but in 1967 to 1972, I just don't know. I would have been surprised if the leading authorities didn't have some sense that smoking was not a good thing to do for patients with heart disease.

Q. When you were in Boston doing your -- your post-medical school training, did you have anything to do with the Framingham study?

A. No, sir, I did not.

Q. Did you ever go to Framingham?

A. No.

Q. Did you ever meet any of the Framingham people?

A. I have subsequently. I don't remember whether I met them then. I know Dr. Kannel and Dr. Castel -- Caselli -- Castelli, sorry. In fact, I believe they're both members of our

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editorial board for Circulation and I invited them to be. So, I have gotten to know them over the years. I don't know them closely. But it's conceivable I met them when I was in training in Boston.

Q. Did they -- did they come to your program to give --

A. If I met them, that would be the way that I met them.

Q. When did the Framingham study determine that smoking was a risk factor for heart disease?

A. Well, we just went through a few minutes ago a manuscript related to that, so you and I could quickly look back at the year and that would be at least one -- one point in time when they were espousing that view. Exactly when they began to espouse that view, you know, I'd have to look back to see. I'm not sure.

Q. That year was 1984, but did Framingham determine that smoking was a risk factor for heart disease prior to 1984?

A. I'm not positive.

Q. All right. What -- when -- strike that.

When was the Framingham study begun?

A. I would have to look back and see exactly when it

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began too, but it is a -- as I mentioned to you earlier, it's a study intending to follow patients over many years and it's deep into that follow-up now. Again, that paper in 1984 would tell us where they were at that time and we can add the subsequent years because there's still follow-ups from that study.

Q. Sure. But I mean --

A. But precisely when it began, I'd have to look and see.

Q. Was the Framingham study going on when you were doing your training in Boston?

A. I'm not positive.

Q. All right. Are there other large studies of people following them as they did in Framingham to determine whether people developed heart disease; and, if so, what the risk factors were?

A. It's the best known. There must be other studies worldwide doing the same thing in countries that I might not be aware of, so my answer to you would be I'm certain there are. There is a study called the ARIC study, A-R-I-C, which has attempted to evaluate and identify risk factors for cardiovascular disease, and it's been in progress for something around five to seven years

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at this time. And it is publishing information regularly, some of it in Circulation, about certain risk factors. It is concentrated primarily on the risk factors for thrombosis, the hematologic vasoactive risk factors. And by that, I mean things like -- this will get into medical jargon, but fibrinogen levels, levels of certain mediators that contribute to thrombosis and so on. It's going to change its focus a little bit in the near future focusing on some of the genetic risks, but in this country, it is another study that one can identify as having similar kinds of interest. I'm not aware that it is focused on tobacco use or smoking so far.

Q. All right. I -- I will ask you about that in a moment, but are there any other studies looking at groups of humans to determine cardi -- cardiology or cardiac risk factors that you can tell me besides Framingham and possibly ARIC?

A. Well, the answer gets a little bit convoluted, but in order to be comprehensive, I need to tell you. There are many clinical research studies being conducted presently. This has become a preoccupation of cardiovascular medicine. Large populations of patients, an example is the TAMI

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group, T-A-M-I, led by Eric Topol, T-o-p-o-l, in which clinical research studies involving 30 to 50,000 patients worldwide have been done and are being done and from the data available in those patients, various things are being pulled out to look at as -- as regards factors like high blood pressure, like smoking, like age, like socioeconomic status, like education that relate to the risk of heart attack. And I gave you that one example. There are others. These are among the largest. But there are studies in Italy referred to as the GISSI, G-I-S-S-I, studies that have accumulated similar data bases. There is a group in the United Kingdom led by Dr. Peter -- Professor Peter Sleight, S-l-e-i-g-h-t, Richard Peto, P-e-t-o, Celine Yusuf, Y-u-s-u-f, that have been also studying very large numbers of patients. Similar kinds of preoccupation is the TAMI group in trying to identify factors that lead to and/or prevent the development of heart attacks. And there are other groups, smaller most of them, accumulating databases of some size and using those databases with an evaluation over a period of years to try to provide information about risk factors. And if, you know, I put my

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mind to it and wanted to create a list and probably spend an afternoon doing it, I could come up with maybe 10 or 15 such efforts.

Q. What does ARIC stand for?

A. I'd have to look to see. It's A-R-I-C and it's a eponym for a series of studies supported by the National Institutes of Health and focused on some of the problems that I mentioned to you. And probably the "RIC" is risk and cardiovascular disease, and I don't remember what the "A" is.

Q. You -- if I recall correctly what you said a moment ago, the ARIC study has attempted to evaluate risk factors, but you're not sure whether they've looked at tobacco; is that right?

A. I'm not certain whether they --

Q. And it was more concerned with the risk factors for thrombus formation --

A. Uh-huh, right.

Q. -- than cardiovascular disease in general; is that right?

A. Well, yeah. This is a focus on the vascular biology generally of the ARIC group.

Q. All right.

A. And that includes, as you say, the thrombus relationship to heart attacks.

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Q. If I wanted to find the publications of the ARIC study --

A. Uh-huh.

Q. -- how would I look for them?

A. One of the premier investigators in the group is a man named Kenneth Wu, W-u, and you could look in the Index Medicus under his name. The ARIC studies would also be identified by title having a certain number of authors' names and then -- for the ARIC investigators. Circulation has published some of the work from the ARIC group over the last three years.

Q. All right.

A. There are several papers.

Q. The -- you also mentioned the TAMI -- strike that.

The ARIC study is done in the United States?

A. By and large. Whether or not it includes any foreign countries, I'm not sure.

Q. All right. Now, you mentioned the TAMI group?

A. Right.

Q. T-A-M-I. Do you know what that stands for?

A. I think thrombolysis and myocardial infarction, but it -- it would be some variation of that name. You have to understand that there might be

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about 500 such abbreviations for clinical research efforts in this country alone right now.

Q. All right. Too bad I can't --

A. One remembers them -- they are abbreviated to keep them simple and one remembers them by these abbreviations rather than by their full names. And I'm not a member of either the ARIC group or the TAMI group.

Q. All right. Framingham was a simple name and it was easier to remember that one.

A. Short. These others are much longer.

Q. All right. Where is the TAMI group?

A. Well, it's led by Dr. Eric Topol and Dr. Rob Califf, C-a-l-i-f-f. Topol is at the Cleveland Clinic and Califf is at Duke, but this includes investigators around the world.

Q. All right.

A. So, there are multiple sites worldwide, but those are the leaders of that effort. There's a -- do you want -- there's another group --

Q. All right.

A. -- called the TIMI group, T-I-M-I. This is -- I hope this has some relevance to all of this.

Q. I -- well, I --

A. This is thrombolysis and myocardial infarction

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studies. Thrombolysis, t-h-r-o-m-b-o-l-y-s-i-s, and myocardial infarction. And that study group is led by Eugene Braunwald, B-r-a-u-n-w-a-l-d. He's at Harvard.

Q. All right. What -- what I'm trying to find out are large epidemiological studies looking at risk factors for heart disease.

A. All right. These -- these study groups didn't begin as epidemiological studies, but what they have done is taken information from the database that they've accumulated in multiple studies in thousands of patients to ask certain questions that are epidemiologically oriented and do relate to risk factors for cardiovascular disease. Very often, they -- the TAMI and TIMI studies have intended to study a certain intervention in a defined patient population and its efficacy or lack thereof in preventing something like heart attacks or the treatment of heart attacks. But as they accumulate these large databases, then they immediately have the opportunity to look at some of the risk factors for heart attacks and other kinds of cardiovascular disease and they're using them in just that way.

Q. All right. So, these would be not -- not like

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Framingham in the sense that that was the purpose of Framingham --

A. Right.

Q. -- but they developed data that could be used in that fashion?

A. That's precisely correct.

Q. All right. And as -- as I understand what -- what Framingham did is they took a group of people, followed them over time, saw who got heart disease and who did not and then tried to figure out what distinguished the people who had heart disease from the people who did not have heart disease?

A. In general, that's correct.

Q. All right. Have these other studies done the same type of thing?

A. They've taken generally patients with a certain kind of heart disease in an evaluation of a particular intervention, as I mentioned, and then they've gone back into their database and tried to look at the associations with that heart disease that the patients had. So, it's Framingham-like in that sense, but it did have a different perspective originally than Framingham.

Q. All right. But these were -- these were -- these

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people did not begin to follow the subjects of the study until after the subjects had developed heart disease?

A. That's right.

Q. So, they weren't prospective in that fashion?

A. No. A couple of things that should be said in answer to your question. They identified patients with a certain problem like a heart attack and they were trying to test in the TAMI and TIMI groups and in this effort led from the United Kingdom by Sleight and Peto that I mentioned to you, they were trying to test a certain intervention in the treatment of a heart attack. They accumulated information about anywhere from hundreds to thousands of patients in the conductance of these studies.

If the -- if the particular study was one of a heart attack, they would have information, demographic information, epidemiological information, that might relate to the risk of that heart attack and they try to elucidate that.

They, in some of these studies, have followed the patients forward from that point and also been able to use certain demographic,

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epidemiologic medical intervention information to try to identify risk factors for new events in the future --

Q. Okay.

A. -- beyond the single one.

Q. Did -- did the TAMI group look at smoking?

A. I think that both the TAMI group and TIMI group have made some analyses of smoking as risk factors for cardiovascular disease. They're not analyses that I participated in and TAMI group has probably published a hundred papers, maybe more by now, of their proceedings. The TIMI group has probably published just slightly fewer. So, there's a lot of work published for those. But certainly the influence of smoking on various aspects of cardiovascular disease has been evaluated in one way or another in both those studies.

Q. All right.

A. And in many studies done by those two groups.

Q. You mentioned the GISSI group in Italy.

A. Uh-huh.

Q. Do you -- do you know what -- what that stands for?

A. I'd have to look back to see.

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Q. All right.
A. It's -- I can tell you what the study is. The study is of patients with heart attacks and it evaluated first the influence of a specific thrombolytic agent, streptokinase, on -- in fact, it was one of the first studies done of the treatment of heart attacks done with a thrombolytic intervention establishing the protective effect of the -- of thrombolysis, namely streptokinase. And there are two or three iterations on the theme from the GISSI group in which they've looked at various aspects that -- clinical aspects that impact on myocardial infarction and the efficacy provided by thrombolytic interventions.
Q. Did -- did the GISSI group look at smoking?
A. I am not aware that they did, but in order to be sure, I would have to look.
Q. Okay. You said there was a group in the UK --
A. Right.
Q. -- led by Sleight and Peto?
A. Sleight, Peter Sleight and Peto. Right. Their focus has been on the treatment of heart attacks too. In their original study, they evaluated -- in one of their original studies, they evaluated

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the influence of that same thrombolytic agent, streptokinase, on heart attacks. And what they showed is that aspirin added a great deal of protection to this thrombolytic intervention, streptokinase, in the treatment of heart attacks. I also have not seen work from their group relating to smoking and cardiovascular disease, but they have an enormous database. And if someone is not evaluating the relationship of smoking to some aspect of cardiovascular disease, I'd be surprised in that group.

Q. All right. But it -- but I take it you're not --

A. I haven't seen --

Q. You're not aware of what findings they might have made?

A. I have not seen anything published from them --

Q. All right.

A. -- about that. That doesn't mean there isn't something.

Q. Have you seen anything else published in England on smoking and cardiovascular disease?

A. The other person who might well have studied the influence of smoking on cardiovascular disease in England is a man named John Deanfield, D-e-a-n-f-i-e-l-d. I really am a consultant to

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you, Mr. Cornfeld. He has studied vascular endothelial function in relationship to a lot of different kinds of interventions. The endothelial dysfunction that I referred to earlier is a -- almost a singular preoccupation with Deanfield and his group and he's been interested in children and endothelial function in adults. And I would be surprised if he hadn't examined some aspect of smoking on endothelial function.

Q. But you're not aware of his findings?

A. I can't tell you where they would be published, but I would be surprised if he hadn't done that.

Q. Are you aware of anything done -- any work done in England on smoking and heart disease by Richard Doll?

A. Spell his name for me.

Q. D-o-l-l.

A. I don't recognize the name.

Q. All right. You mentioned the TIMI group which looked at thrombolysis and myocardial infarction. Where is that group -- where do they do their work?

A. Well, it's led by Braunwald out of Harvard. And there are multiple centers first in this

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country. Originally our own group helped him some while I was in Dallas and still while I'm in Houston. And there were some originally 10 to 20 other groups, today probably 70 or 80 other groups worldwide that help him. And that work's been published at least in a hundred separate articles and journals throughout the world, but includes Circulation and New England Journal of Medicine.

Q. Did that group look at smoking?

A. That, again, has not been a singular preoccupation of theirs, but I do believe that if you look back through the TIMI publications or got a list of them, you would find that there's some so-called substudies looking at the influence of smoking on various cardiovascular abnormalities which comes out of their database.

Q. I take it, though, you cannot tell me what their findings have been, if any, regarding smoking?

A. I didn't come prepared to do that today. It's not right at the top of my mind.

Q. Okay.

A. I know the TIMI studies very well and the substudies, little studies, that come out, unless they differ -- this -- this would really be the

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thing to emphasize to you. Unless they differ from the body of information that I'm aware of relating smoking to cardiovascular disease, I wouldn't necessarily pay much attention to them and I don't because they are just confirmatory information for a body of evidence that's already existent. Now, if there's something strikingly different from that, then I'm very likely to remember it.

Q. And -- and so I take it you don't recall what those of the TIMI --

A. I -- I'm aware -- I am aware -- as I tried to say, I am aware that -- that the TIMI group and TAMI group have some publications relating to the influence of smoking on various cardiovascular variables and parameters. That was not the singular purpose of their evaluation, but something that has come from their databases as part of a substudy of a bigger study. In general, I believe the results con -- conform to the existing belief of mine and others that smoking and tobacco are very injurious to the cardiovascular system, especially blood vessels. Is there any exception to that in anything that is published? That, I would have to look and

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see. Any single exception, that, I would have to look and see.

Q. All right. There could be aspects of that issue that a study could deal with beyond just the general proposition of whether smoking is injurious to the cardiovascular --

A. Yes, sir.

Q. -- system?

A. That can be.

Q. All right. For example, it could look at the amount of smoking it would take to be injurious. It could look at the specific type of injury. It could look at the combination of smoking with other factors and I'm sure it could look at other aspects --

A. Right.

Q. -- of smoking?

A. There are many other things that might be examined.

Q. Okay.

A. We can agree.

Q. All right. And -- and there have been studies that have looked at a wide number of aspects of the smoking and cardiovascular issue; isn't that right?

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A. Yes, yes.
Q. All right. Are you aware of any other studies like Framingham where they set out specifically to find risk factors for heart disease by following a group of people?
A. Well, I think the ARIC study has done that. I think that is something that it is doing. And -- you know, I know it's doing that because we also have -- well, you won't care, but we have access to a large number of blood samples from the study that we want to use to try to define certain genetic risk factors --
Q. Okay.
A. -- for cardiovascular disease. So, that's an ongoing evaluation the same way, a little bit different, than the Framingham. And there will be others. I -- I'm not proposing myself as an absolute expert on a categorization of every single study that is done epidemiologically --
Q. Sure.
A. -- to identify risk factors in cardiovascular disease. I've heard of most of them and if I sat and thought about it just a little bit, I can give you a broader list, but I didn't come here thinking I -- I might do that.

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Q. Have you given me the list of studies that you're familiar with?

A. That I'm familiar with, probably not. That come immediately to mind, yes.

Q. Okay. Are you aware of any studies that have found in any particular group of people that smoking does not have an injurious effect?

A. I have certainly seen rarely, very, very rarely, a publication that surprises me a little bit about not being able to demonstrate something that I would expect to be able to show based on a body of information that exists. I'm talking generically, but I'm going to answer your question. And smoking is not an exception for that. So, the answer to the question would be I have seen, from time to time, something in the literature. I've seen something submitted to me as the editor of Circulation where a particular practice doesn't seem to show what 500 other studies have shown. And my reaction to that is "What's wrong with that study?" And I look at it to try to determine what's wrong with it. A study is no better than the people who do it, no better than the numbers of individuals that are evaluated in terms of how representative it is,

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this, that or the other, and some of them failed to take into account many other things that are operative in that milieu which might hide the impact of a particular intervention. So, that's a very long-winded answer, partial answer, to your question if you'll forgive me for it, but I want to be clear about this.

Q. All right.

A. I have, on occasion, seen something that smoking was not associated with a magnitude of risks that I've come to expect from a large number of other studies, and I think that may be true in a -- in an interaction with thrombolysis specifically. I think as you look at the TIMI and TAMI studies, when you do that, I think you may find a substudy or two that suggests that patients who smoke in that immediate thrombolytic period, thrombolysis being the lysis of a clot from an intervention, the clot having caused the heart attack, that in that immediate thrombolytic period, that the use of smoking previously is not associated with the kind of adverse events one might have expected. There are at least one or two publications from the TAMI or TIMI group which will generically deal with this kind of thing. This is not

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different from what I said to you a minute ago. I told you I thought you would find some work like that. Exactly where it is and when it was published, I would have to go and look for it, but I'm aware that that exists. Even the people that wrote the article were somewhat perplexed.

Q. Can I see if I understand what -- what you just told me?

A. If you can't, I'll help you.

Q. I -- I hope you will. But if I can put it in words that a lawyer uses or at least --

A. I'm not sure I want to do that, Mr. Cornfeld.

Q. -- is familiar with -- is familiar with. When you -- when you use the term "intervention," you mean some kind of treatment?

A. Yes.

Q. All right.

A. And I was talking about thrombolytic intervention, lysis of the blood clot --

Q. Sure.

A. -- has led to a heart attack.

Q. You're talking about when you give a patient who's had a heart attack a certain drug --

A. Right.

Q. -- is that right? And what -- what you're saying

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is that there are some studies that would show that whether or not that patient smokes does not affect the effectiveness of that treatment; is that right?

A. In general, yes.

Q. All right. And that -- and -- and those papers come out of the TAMI and TIMI work?

A. They do, out of substudies related to that work. And you'll have a hard time finding them because there aren't many, but there are one or two with -- that -- that show those kinds of data that left everybody in the cardiovascular community somewhat perplexed.

Q. Why were they perplexed?

A. Because I don't think they really believe it.

Q. Are there other studies that show that smokers don't do as well after thrombolytic treatment?

A. You know, I think the fundamental problem is there aren't very many studies that address that particular point in great detail with adequate numbers and statistics and follow-up and sensitivity of evaluation that would allow one to say, "This is right" or "wrong." That's me. Sorry. So, these were substudies, very limited studies, that just -- I remember them because

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they fit into that category that I mentioned a minute ago in my unfortunately long answer to you where there is something that deviates from a great body of evidence in its finding. That's what I tend to remember.

Q. All right. What -- what I --

A. And -- and there are a couple of articles like this.

Q. All right. And -- and so this is an area where the field of cardiology is doing additional work to see if this really --

A. Well, I'm not --

Q. -- is a valid finding?

A. -- I'm not -- I'm not sure they are. I'm not sure -- I'm not sure they are. I'm not. And I'm not sure too many others are because it's a -- that's a very hard thing to look at in the midst of this milieu. Also as part of my long-winded answer a minute ago, I mentioned -- and I'll try to make it simpler now -- that when you -- when you evaluate an intervention like lysing a blood clot with a drug and you've got the patient who's very sick with a heart attack, there are so many things going on in that patient. Their blood pressure is variable. Their heart rate is

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variable. They're in a lot of pain as a consequence of release of catecholamines and many other substances that modify cardiovascular events, endogenous steroids, so on. I won't bore you with a list of it. But it -- it's a very difficult time to study an intervention that has some -- might have some effect when you're contrasting that effect with other things that are going on internally and medications that you've given the patient which are -- are intended to be protective. So, you're looking at contrasting influences and are reaching a conclusion about benefit or detriment of something that's in the background of this patient that they're not actively doing at the moment is really difficult to do. The patients with heart attacks aren't actively smoking at the moment. One's talking about their past background.

Q. You will --

A. So, it's a tough thing to study. That's the bottom line.

Q. You will give a patient that treatment whether or not the patient is a smoker?

A. Yes, sir.

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Q. And I take it you would advise that patient after recovery and after he leaves the hospital to stop smoking?

A. I always do.

Q. All right. So, whether or not his smoking status has an effect on the effectiveness of the thrombolytic intervention, I guess, doesn't really make a whole lot of difference in terms of treatment of the patient; is that right?

A. Patients with certain kinds of heart attacks are treated with thrombolytic intervention without -- without contraindication. If their blood pressure is high, you can't do it safely but, otherwise -- or if they have some bleeding risk and a few other things. But smoking itself is not a contraindication to treating a patient with a thrombolytic intervention. One expects benefit from the thrombolytic intervention and the reason that the -- I would advise someone not to smoke after the heart attack doesn't have very much, if anything, to do with the thrombolytic intervention. It has to do with trying the prevent the progression of their vascular disease --

Q. Okay.

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A. -- or a new heart attack.
Q. Then -- Doctor, let me return to the question I asked you earlier.
A. Go ahead.
Q. Before I do, do you need to answer that?
A. No. It can wait.
Q. Okay.

MR. CORNFELD: The record should reflect the doctor was beeped and that's what we're referring to.

A. Paged.
Q. (BY MR. CORNFELD) Paged. Sounded like a beep to me.
A. It is a beep.
Q. Okay.
A. That's what we refer to it as, a beep, but I was paged on my pager.
Q. All right. Are you aware of any studies that indicate that smoking is not a risk factor for heart disease in any particular groups of people? I don't mean about the -- with respect to the issue of thrombolytic treatment, but -- in -- in Framingham, it was, but maybe in some other city, it wasn't or maybe --
A. Okay.

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Q. -- left-handed piano players or maybe Eskimos or I don't know.

A. I -- I understand your question and I would answer it by saying if -- in this way: If one made a diligent search of the cardiovascular literature, I would be very surprised if you couldn't find a manuscript somewhere that suggested that smoking was not detrimental in some population. As you say, left-handed piano players, one with one finger or a missing ear or something like that. But it doesn't seem to me that one should be terribly impressed by a single dissenting or very few dissenting points of view or data pieces when there's an enormous body of evidence that suggests the major risks that smoking have for cardiovascular disease.

Q. Are you aware of any studies looking at the effect of smoking on the cardiovascular systems of Hispanics?

A. Hispanics?

Q. Yes.

A. That population of individuals is evaluated demographically. In most clinical studies, it would assess the impact of smoking on cardiovascular disease where there's a multi-

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national group included. I'm not aware of a publication that says that smoking is advantageous in Hispanics or useful to their cardiovascular system. I'm not aware of such --

Q. That wasn't my question. I'm sure there's no publication by a cardiologist that says smoking is advantageous to the -- to the cardiovascular system of anybody. What I'm just asking about now is: Are -- can you point me to any study or studies that have looked at the effect of smoking on the cardiovascular system of Hispanics?

A. Specifically?

Q. Yes, of any type of Hispanic population, whether we're talking about Hispanics who live in Texas or we're talking about Hispanics who live in Spain or who live in Mexico or Argentina or Puerto Rico or anywhere.

A. There are -- I would have to look to see if smoking -- smoking is included in the study I'm going to tell you about, but there is -- there are studies from my medical school, the University of Texas Medical School at Houston, its school of public health, evaluating the Hispanic population on the Gulf Coast and their risk factors for cardiovascular disease. It is

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focused heavily on lipids primarily. That's been the focus. What is the relationship of cholesterol, LDL, HDL to risk of coronary disease among the Hispanic population. It's in the Corpus Christi area.

Q. Okay.

A. And I would be very surprised if there's not an independent evaluation of the influence of smoking in that population. I have not read those papers carefully. They're only a few, only a handful.

Q. Doctor, may I interrupt you for just a moment?

A. Yeah.

Q. I will ask you about that study. First I want to find out if -- if there are any others you can point me to.

A. Okay. That focus specifically on that population?

Q. On any Hispanic population.

A. Yeah. There aren't, but if I wanted to find them, I would go into the literature in Spain of cardiovascular medicine and in Mexico and South America to look for the same thing. And I'm sure you can find some that would be in Spanish and -- and Mexican, probably, by and large.

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Q. All right. Then --
A. And I don't read them regularly, though I do speak Spanish.
Q. Okay. Doctor, the -- then let me ask you again about this University of Texas study in the Corpus Christi area. Do you recall who the author is of that study?
A. One -- one of the -- one of the primary authors will be a man named Darwin LaBarthe, L-a-B-a-r-t-h-e. He's in the School of Public Health at the University of Texas Medical School at Houston. Another person who's helped with that work is a man named Dr. Phillip Orlander, O-r-l-a-n-d-e-r, and he's at the University of Texas Medical School at Houston.
Q. Okay.
A. Some of that work is published in Circulation in the last three or four years. As I said, its preoccupation is on lipids primarily, but it looks at multiple risk factors.
Q. What did -- what did that study find with respect to the lipids?
A. It shows the expected relationship of elevated cholesterols and LDLs, low HDLs, to risk of atherogenesis among this population. It also

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examines diabetes and the risk of cardiovascular disease. Diabetes is relatively frequent among the Latin American population, as you probably know. And it has a very adverse effect on blood vessels. I believe that you'll find some assessment of smoking and its influence on atherogenesis in these papers that we are talking about.

Q. Did that --

A. And I guess the fundamental question would be whether smoking -- this is -- this is a population that's heavily diabetic and minority and Latin American. And the question will be whether smoking has an additive effect to vascular injury over and above what diabetes does or hyperlipidemia does. And that's a subject that would be of interest to study further. And you might find variable -- variable things.

Q. Are you aware of -- strike that.

Did that study look at the prevalence of hyperlipidemia in the Hispanics --

A. I believe it did.

Q. -- on the Gulf Coast?

A. I believe that it did.

Q. What did it find?

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A. Well, again, this is a diabetic population and it's a population who's -- it -- it -- it found that hyperlipidemia is pretty common among the Latin American population, especially among the diabetic Latin American population.

Q. All right.

A. And this population is a little different than some others because of the influence of diabetes. There's a little different socioeconomic background and, also, it's a group of people who are not highly educated in the importance of diet and other risk factors for cardiovascular disease. And it's -- the overall intent of this kind of study is to not only identify the specific risk factor relationships among them, but to try to change them, to try to educate them, to try to help them.

Q. Doctor, let's -- let's back up from these issues and -- and talk just generally about you and your career. Professionally, I gather from what you've told me that you've been involved in patient care; is that right?

A. Yes.

Q. Research?

A. Yes.

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Q. Teaching?

A. Yes.

Q. All right. Can you tell me what percentage of your time is made up of the various types of activities that you have engaged in?

A. Well, let's start with clinical care since that would be most relevant to our discussion today. And I've been involved in taking care of patients with medical diseases, including heart diseases, since 1963 late in my medical school career to the present. And I've been involved in taking care of patients with heart disease since I began my medical residency, which was 1965. And then I have concentrated on the care of patients with heart disease not exclusively, but it's been my preoccupation since 1969. I personally have somewhere between 900 and 1,000 private patients that I am responsible for their care. Many of them have my beeper number and use it. At Hermann Hospital, which is the teaching hospital of the University of Texas, for the last almost eight years now, I have led one of the medical teaching teams and I see patients on that team with young doctors. This is in my role as an educator and physician on a daily basis. In my

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role as the medical director and chief of cardiology at the Texas Heart Institute, I'm involved on a daily basis with one of the largest efforts in the care of patients with heart disease in the world, patients with all kinds of heart disease, every imaginable kind of cardiovascular disease. And I guess on paper, I'm overall responsible for their care.

Q. What per --

A. I --

Q. I'm sorry.

A. Let me just finish and I'll do it quickly. It's hard to separate the work as a doctor and the work as an educator because I've often got young doctors along with me. So, whatever -- of all stages of training or I'm in a meeting where something is being presented, we have periodic conferences, daily conferences, lots of young doctors. So, it's hard to separate the care and the educational efforts. I've always been involved in cardiovascular research ever since I focused on cardiovascular disease. I've been actively supported with research grants from the National Institutes of Health on a continuing basis since 1974. I have three active NIH

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grants, have been supported by some other kinds of research support too. So, my day -- as a division of all these things, my day is an -- about a 18 or 19-hour day, usually six days out of the week and another seven hours on Sunday, something like that. And it's divided between these things. I can't separate the care and education, the research, actual time I spend thinking about, writing about, directing, reviewing research, probably about 25 or 30 percent of my time, the rest in clinical care and education. And the editor part of me for Circulation is mixed into the -- to the day.

Q. Okay. How many new patients do you see a week, in a typical week?

A. It's really highly variable, but I would say I see a minimum of five new patients a day and it may be as many as 10 to 12 new patients a day. And then, of course, there are a similar number of follow-up patients. It varies a lot. It just depends day to day.

Q. And these are patients with heart disease?

A. Either they have heart disease or they're presumed to have heart disease. Sometimes they're sent to me with a designation of heart

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disease and they don't have it.

Q. All right. For how long have you been seeing exclusively patients who either have heart disease or are presumed by another physician to have heart disease?

A. Okay. Remember, it's not exclusive because I am a -- I'm an internist too. I'm a cardiologist and internist. And in my role at Hermann Hospital, I'm the chairman of medicine there. So, I see patients with heart disease and -- and medical diseases both there. So, it's not exclusive in any sense. But I've been seeing patients with cardiac diseases since I was in medical school, the third year of medical school. That would be 1963. My medical school was in the Texas Medical Center here in Houston, with is probably the largest medical center concentrating on heart disease in the world and I was involved in that.

Q. How many patients do you see as an internist who have something other than heart disease or presumptive heart disease?

A. On a daily basis?

Q. However it would be best for you to describe it.

A. Okay. On a daily basis, five to ten on a daily

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basis.

Q. What problems do you see them for?

A. Everything imaginable, every single thing imaginable. Ulcers, lung disease, diabetes, hypertension, dementia, leukemias, cancers, upper GI bleeding, everything imaginable. Now, let me just hasten to say in those areas where I'm not -- where I'm not a real expert that I enlist the help of specialists in those areas in the care of those patients. So, in those instances, I serve as a generalist. I am the specialist for the cardiac disease.

Q. Have you -- have you tried to compile or to estimate the percentage of patients that you have seen with different types of heart disease who are smokers or who have hyperlipidemia or who have hypertension or who have a family history of heart disease or who are overweight or have any other risk factors?

A. No. I've never made any effort to compile a list of such. I see large numbers of most of those categories.

Q. All right. And I -- I take it, then, you have also not tried to see how the prevalence of any risk factors in your patient population would

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compare to a comparable group of people without heart disease?

A. I care for patients with heart disease. And so my focus is on -- I care for patients with heart disease or those who are concerned that they may develop heart disease, some of whom don't have it. As we just agreed a minute ago, for some who are thought to have heart disease and don't and for some who are at high risk of heart disease because of their family histories who are still very young. Occasionally, I see a child with some kinds of -- with some kind of cardiovascular disease. So, I really see -- and then I see these patients with all kinds of medical diseases some of them who don't have heart disease at the time. I really think that as much as any physician does today, probably anywhere, I see a very broad spectrum of medicine and cardiovascular disease. And I have not limited my efforts in cardiovascular disease at all.

Q. All right.

A. I want to see everything possible.

Q. Sure. But my -- the focus of my question had to do with -- with whether you can tell us -- because you've made an effort to determine how

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the presence of different risk factors would compare in your population to comparable populations without heart disease.

A. I'm not involved in such epidemiological studies.

Q. All right. I assume you -- you advise your patients not to smoke?

A. As I mentioned before.

Q. All right.

A. I do.

Q. Yeah. For how long have you been doing that?

A. For some years, and I don't know how many. I -- you know, it's -- as we discussed before, it's hard to remember the exact point at which one started to do something in a career that's some 25 to 30 years in an area, but for a number of years. It's not recent.

Q. Can you recall a period of time in your career when you did not advise patients not to smoke?

A. No, I cannot, but I am certain that as I began my career in medicine and cardiovascular disease, I did not insist as strongly on their not smoking or try as hard to persuade them not to smoke as I have in the last years.

Q. What led you to change the way you advise patients in that regard?

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A. My conviction that smoking is very harmful to the cardiovascular system, especially the blood vessels.

Q. What was it that you learned that led you to do that?

A. Well, we've -- again, with all due respect -- I know you want to pursue this, but with all due respect, I've -- I have answered that before and I answered it by saying it was the sum of my experience in caring for patients with heart attacks, unstable angina -- that's a threatened heart attack -- strokes, coronary artery spasm, my experience in caring for the large numbers of those patients over many years now, my experience with the clinical research studies that we have discussed, and my experience in hearing about the work of others and reading about the work of others both as a reviewer of their work, manuscripts submitted for publication, and many meetings and personal discussions with leaders of cardiovascular medicine worldwide and as an editor. It's the sum, it's the totality of all of that.

Q. Doctor, there was some point in your career when you went from advising patients in a fashion that

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is not as vigorous as it is today --

A. Yes.

Q. -- not to smoke to advising patients very strongly not to smoke, and what I want to try to find out -- I know you can't tell me the date and the time on which that occurred, but what I would like to know as much as I can -- as close as we can get it when that happened and what was it. I know -- I know you've -- you have a lot of things in your head, but was it Framingham, was it one of these papers in front of us, was it -- was it what a -- what a --

A. It was not any --

Q. -- respected professor said?

A. No. No. It was not any single thing. It is the totality of that. And -- and I -- you know, I guess it's just hard to explain, but it's, I also think, reasonably self-evident that involvement in an area of work and having a certain number of personal experiences -- this would be the care of patients -- seeing many different things that relate to a particular problem of all kinds, one finally has virtually every single doubt removed or every single bias confirmed or one comes to become -- to be an advocate of something based on

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the totality of that experience. And you must have had this experience before that something like this must have occurred in your professional career where based on exactly the same things, you've come to -- to believe very strongly in certain principles or points. This has to do with medical risks for me. But it wasn't a moment. It wasn't a person. It was not a paper. It was not a single patient or observation. It is all of it which is overwhelming, absolutely overwhelming and leads me to become an advocate for the cessation of smoking. I'm absolutely certain it would have a major beneficial effect in reducing heart attacks and strokes and peripheral vascular disease, among other things.

Q. Doctor, I take it, then -- well, strike that.

Was there a time before you believed that the evidence was overwhelming when you believed that the evidence -- that some evidence was there, but less than overwhelming when you strongly advised your patients not to smoke?

A. There would be two things now. One would be a stage in my becoming a doctor when I was naive, more naive than I am now and not as

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knowledgeable, not as experienced. So, whatever I believed or didn't believe at that point probably isn't worth spending much time on as compared to after many years of experience in all the ways we've talked about. So, I've got to try to separate that early period in my career knowing I didn't know as much as I would need to know to be an advocate or not an advocate about this issue from when I actually started to learn and -- and develop firm convictions. It is not recently, as I've tried to explain, that I developed this conviction. It is over a number of years now. How many years has it been since I became a firm advocate? It's very hard to know, but certainly in the last seven or eight, I've become a very firm advocate. There's one other point we should try to agree on that I would emphasize. The evidence about the injurious effects of smoking related to the cardiovascular system has been developing throughout this time. Some of the insights that exist right now did not exist 25 years ago or 30 or 50 years ago. This has been a progressive thing too. So, there's some meeting between when one becomes knowledgeable enough, experienced enough and when

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a body of information is developed enough to let those two things come together to allow opinions to be formed, whatever they are.

Q. Am I correct in this, then? That the effect of smoking on the cardiovascular system is nothing that got written in black letters in a medical book and you looked at it and said, "Aha, that must be the case," but rather it was a process that you went through applying your expertise to everything you know as a doctor and exercising your own personal judgment as a doctor; is that right?

A. That is correct, plus patients that I've seen --

Q. I -- I meant to include that in what you know.

A. -- presentations that have been made. All you've said and all I've said --

Q. All right.

A. -- has had the sum impact on me.

Q. So, you -- you applied your expertise and your judgment to what you learned from patients you had seen. You applied your expertise and your judgment to what you heard at -- at seminars and at meetings of other doctors. You applied your judgment and your expertise to what you read in medical journals and everything else that you

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know, Dr. James Willerson, as a doctor; is that right?

A. I think generally, yes.

Q. All right. Do you advise patients who you see as an internist not to smoke?

A. Yes.

Q. Do you -- do you tell every patient that?

A. Yes.

Q. Whether you see them for something that might be related to smoking or not?

A. Yes.

Q. Do you ask every patient whether he or she smokes?

A. I try to.

Q. All right. For how long have you been doing that?

A. Years. We have the same problem in my being decisive about a moment.

Q. Sure.

A. For years.

Q. This is not something you did recently?

A. Just recently, no. Recently, yes, not just recently. I do it today.

Q. All right.

A. And I've done it for years.

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Q. Have you done that, advised every patient you see not to smoke, for the majority of your medical career?

A. What would the majority of 25 years be? The majority of 25 years would be 13 years. Have I done it for 13 years? I don't know whether I've done it for 13 years every patient I've seen. For some years, something approaching 13 years. Certainly in the last seven or eight I've attempted to do it with every patient that I've seen that I know smokes.

Q. Are you familiar about the Surgeon General's reports on smoking and health?

A. I haven't read it recently. I was aware of the publicity of it, about it, when -- this would be Dr. Koop's statement. This is one that developed under C. Edward Koop.

Q. What are you familiar with that Dr. Koop did?

A. That there was a general advisement that smoking may be injurious to your health. That's a label that subsequently was applied to cigarettes and I think he's primarily responsible for it.

Q. Are you aware of any statements that the Surgeon General has made regarding smoking and the cardiovascular system?

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A. Is this relevant to -- to my opinions?

Q. I'm -- my question is: Are you --

MR. CORNFELD: Well, would you read back the question?

(The question was read by the reporter.)

A. Yes. I -- I know you want me to answer that and I'll -- I'll try if you -- if you require. I really would -- I really would ask you with all due respect if you'll ask me a specific question about that, I can tell you "yes" or "no." If you ask me if I'm aware of any statements that have been made, of course I'm aware of some statements. But you may have something specific in mind and the statements that I'm aware of in general are those that I mentioned. Certainly from Koop there was a -- a general emphasis on the fact that cigarette smoking may be injurious to one's health and he had in mind the cardiovascular system and lungs. I've met him. I know him. He's not a friend of mine. I know that he feels that smoking is injurious to one's health.

Q. (BY MR. CORNFELD) When was Koop Surgeon General?

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A. Several years ago.
Q. Are you -- but by "several," what do you mean? Do you know under what President?
A. He was Surgeon General ten years ago. He was Surgeon General up until about five years ago -- these are approximate dates -- four years ago. So, he was Surgeon General during -- I believe during part of the time that Bush was President and possibly part of the time that Reagan was President.
Q. All right. Prior to that time, was there a Surgeon General who looked at the issue of whether smoking has an effect on the cardiovascular system?
A. I sure hope so, but I'm not certain.
Q. All right. The first time you're aware of a statement by the Surgeon General on the effect of smoking and the cardiovascular system would be under Koop?
A. Yes.
Q. Sometime within the last ten years?
A. Yes.
Q. All right. Is there a label on cigarette packages that refers to the cardiovascular system or has there ever been?

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A. I have not looked to see personally. I believe that cigarette -- cigarette packages and cigarette vending machines have a label that says "The Surgeon General wishes for you to be aware that these may be injurious to your health." I -- I'm not aware that it focuses specifically on cardiovascular health, but is a more generic phrase, but I -- I haven't looked at this recently. I -- you know, it's not something that I can do anything about. If -- I'd like to word it -- if I worded it -- let me answer it this way. If I worded it, every single package of cigarettes would say, "This is injurious to your cardiovascular health" if I were the Surgeon General.

Q. Do you believe smoking should be banned?

A. This is just a personal opinion. Yes, I do.

Q. You believe that no one should have the right to smoke a cigarette?

A. I'm really not here as an ethicist or a legal inter -- an interpreter of the Constitution or legalities of a variety of different kinds. I think all people have rights. I answered your question about whether it should be banned as a doctor, not as someone who's an expert on the

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Constitution. I'm not a lawyer. I'm just a poor doctor. I wish they were banned. I wish they were banned because we would reduce the risk of heart attacks and strokes and a variety of other things, some of which are very, very serious markedly by stopping people from smoking. My job as a doctor is to protect people's health. That's what I promised I would do. And if you ask me if I want cigarettes banned and I tell you anything other than "yes," I'm not a doctor of my conviction and I'm not a doctor who cares about people. Of course, I believe people have rights and I'm not trying to get into a discussion with you or a disagreement about rights versus medical priorities or the benefits of -- for medicine and people's health versus individual rights. I wish cigarettes could be smoked, so I'll reword -- I -- I'm sorry. I wish cigarettes could be banned.

THE WITNESS: Please correct that for me.

A. (Continuing) I wish cigarettes could be banned from the face of the earth.

Q. (BY MR. CORNFELD) Tell me the other risk factors for heart disease that you're aware of besides

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cigarettes.

A. Genetic risk is an important, high blood pressure, elevated serum cholesterols and LDLs, low HDLs, increases in oxidized LDL, increases in lipoprotein little a, Lp little a, diabetes mellitus, homocystenemia, cocaine abuse. We're talking about risk factors in coronary disease, are we not?

Q. Yes.

A. Is that the prospective?

Q. Well, was there some other?

A. No. I just want to be sure that I was still -- aging, hypertriglyceridemia, sedentary life-style. Put smoking right at the top of the list with genetics. I think the two of them lead the list.

Q. Are there any others?

A. Probably.

Q. Are there any others you can think of?

A. You want a whole page, don't you?

Q. If we reach the bottom of the first page, we can go onto the second page.

A. I'm sure we could. I'm sure we could. These are the major recognized risk factors for coronary vascular disease as of September the 7th, 1997.

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There will be others listed.
Q. How about obesity?
A. Well, it's very controversial. I started to list it. I honestly believe it's very controversial and my own opinion is that in the absence of insulin resistance, hypercholesterolemia, sedentary life-style, hypertension, that it probably is not a major risk factor, obesity, per se.
Q. How about -- how about diet?
A. Well, that impacts as it influences cholesterol levels.
Q. So, diet would not be -- a high fat diet would not be a risk factor --
A. Yes, it is.
Q. Excuse me. Let me finish.
A. I'm sorry.
Q. Unless it affects cholesterol?
A. No. Diet would be -- I apologize for interrupting you. Diet would be a risk factor insofar as it influences cholesterol and triglyceride concentrations, the two of them, and insofar as it influences body weight which influences high blood pressure which influences sedentary activity, it is a factor, but it's

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through several other things rather than as a specific as we know it today.

Q. Have you seen the reports of studies that find that a high fat diet is an independent risk factor meaning independent of its effect on cholesterol?

A. Yes. A high fat diet is often listed as a -- as a risk factor, but I -- in my opinion, it is through -- generally through the cholesterol/triglyceride influence.

Q. So, you would --

A. And -- and the weight/blood pressure/sedentary life-style.

Q. So, you would --

A. I advocate a low fat diet.

Q. You would disregard studies that find that a high fat diet is a risk factor independent of those other risk factors?

A. No, I would not disregard them. I didn't say that. I said my interpretation of them, my belief is based on my own interaction with all this for a long time, that that risk is, in fact, transferred in the ways that I mentioned.

Q. When -- when --

A. Independent risk factor is a result of a

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statistical analysis of one side or another. There's no perfect statistical analysis. There's no perfect way to dissect among all of those things. On a very high fat diet, it's pretty hard not to gain weight. It's pretty hard not to influence blood pressure and it's pretty hard, if not impossible. It's -- it's possible, but it's un -- it's unusual not to influence serum cholesterol and LDL for some people with genetic counter-regulatory factors that allow them to keep their cholesterol normal even though they eat a lot of fat, but in general, I think the risks are transferred that way. That's my opinion and I'm not disregarding anything.

Q. Would -- would -- then would it be the case that -- you said -- you -- you referred to statistics a moment ago.

A. Uh-huh.

Q. A statistical association by itself doesn't prove either that something is or is not a risk factor or that something is or is not causative without also your applying or some other expert applying his or her own professional judgment; is that right?

A. Statistics or analyses that suggest certain

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things done very carefully in adequate -- adequate numbers of individuals that are truly representative of a group at risk, they provide important insight. Proof that something does this or doesn't do that comes from the evaluation of that specific intervention in a certain setting and the identification that that is associated with the development of some abnormality. And failure to use that or do that is associated with a much reduced risk. And that too would be in large numbers of people that are representative of the general -- general population at risk. So, one has to be careful with statistics. One really needs to be an expert with statistics in order to evaluate them and know the shortcomings and advantages in any particular evaluation.

Q. And apply one's own expert judgment, correct?

A. If one's really an expert.

Q. All right. Doctor, you said you advocate a low fat diet in your patients?

A. I advocate a low cholesterol, low cholesterol diet. I -- in those who are hypertensive, have high blood pressure too, a low salt diet. And in those who are diabetic, a diabetic diet. And in

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those who are overweight, a weight-reducing diet because of the impact of weight on a number of other variables that I believe have an adverse influence. The low fat is part of a low cholesterol diet and it's intended to help keep cholesterol and triglycerides as low as possible by dieting. That's not always adequate, of course, by itself.

Q. Now, do you do this for your patients who are not just cardiac patients, but your internal medicine patients?

A. I do it for cardiac patients and -- who have vascular disease or who are at risk for vascular disease. I do it for internal medicine patients who are similar, who are at risk for -- who are at risk for or actually have vascular disease. You know, most of the patients -- cardiovascular disease is so prominent that most patients with other kinds of medical diseases have some kind of cardiovascular disease. The majority of them do.

Q. If -- if you have a -- a -- an internal medicine patient who comes in to see you for something unrelated to the cardiac system, say, comes to you for the flu, and you note that he is overweight, do you advise a weight-reducing

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diet --

A. Yes.

Q. -- or a low fat diet?

A. I advise a weight-reducing diet which will include usually a low fat diet.

Q. All right. And you tell him that because he is overweight he is at increased risk for heart disease?

A. I tell him that because he is overweight, he is at risk for increases in blood pressure, that that has an impact on his cholesterol and LDL value and has an impact on his insulin sensitivity and carbohydrate tolerance. It may have an impact on how active he can be, sedentary life-style, and a number of other things that are outside the cardiovascular system. People are very overweight. Your question, I -- I suppose, presupposes a very obese person, not somebody who's just a little bit overweight.

Q. Actually, I -- I didn't have either one in mind.

A. Well, I'm talking about someone who is considerably overweight, not just a little bit overweight. But considerably overweight has an impact on function of the lungs as well and so -- and their sense of self-esteem and a variety of

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things like that. So, there are lots of reasons to recommended a weight-reducing diet. In somebody at risk for cardiovascular disease or with cardiovascular disease, even if they've got another problem, they come to see me and they're overweight, I recommend they lose weight because I think it will bring their cholesterol down.

Q. Doctor, what -- what do you consider to be the kind of gross overweight that would cause you to advise a diet just because of the patient's weight?

A. Well, there's a -- a visual assessment that's involved in there, so there's some -- a little bit of subjectivity to it, but certainly somebody who is 50 pounds or more above what might be healthy or idealized weight for them I think is probably too heavy for their -- for their health.

Q. What -- what constitutes the low cholesterol or low fat diet that you advise for a patient?

A. Well, it's a diet that's predominantly fish and chicken and a diet that avoids regular milk and eggs and bacon and sausage and red meat. It's a diet that avoids pies and cakes, candies and really emphasizes vegetables and fruits and, as I said, fish and chicken, skim milk.

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Q. Is there a calorie amount per day?
A. Not -- not -- as I do it, not necessarily, unless they're overweight. If they're badly overweight, there is a calorie amount, and that calorie amount might be anything from 1500 to 1800 calories a day depending on the -- how much overweight the individual is.
Q. Is there an -- an amount of fat that you would say would be the limit somebody should have if they're --
A. I really -- there are some physician specialists who emphasize an amount of fat. I really personally rely on a kind of diet rather than an amount of fat. Like any area of endeavor, different specialists have different recommendations and I have a colleague who recommends sawdust effectively, sawdust for meals. Do you understand what I'm saying to you?
Q. I think I do. I'm -- I'm wondering whether I should ask your colleague's name and maybe I'll try it.
A. I won't tell you. But it's a diet -- my point is generically while trying to be humorous that it's a diet that's so unpalatable and so rigid in its

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fat content that many patients don't go back to see this physician a second time and they begin to joke about the physician and don't take it very seriously. There is some balance between what one might do ideally and what a patient is likely to follow and still be protected. So, my own preference is to talk very generically about those foods, identify those foods that are very low in cholesterol and, if necessary, salt and a certain caloric restriction if I think that will be helpful. Beyond that, if I want more precise information, I refer a patient to a dietitian to have them become involved and help them plan their meals very specifically. Sometimes I do that in somebody who can't seem to lower a modestly elevated cholesterol down into a normal range who's also overweight who should be able to normalize that cholesterol just by dieting without having to take a medicine. So, I take a try first. And if that doesn't work, then I enlist the help of a dietitian.

Q. Is -- is a low fat or a low cholesterol diet a good idea for everybody, not just people with -- with heart disease?

A. From the perspective of trying to prevent heart

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disease, in a very generic sense, it's a good idea, but you would rob a certain number of patients from a very pleasurable life-style. Take Winston Churchill. I have that prototype in mind of someone who basically could do almost anything they wanted and still live to a ripe, old age and enjoy the life and not have a heart attack at a young age. It depends on lots of things. And I think to have one prescription about diet for everybody wouldn't be the right thing.

Q. How would -- how do you determine whether somebody is one who should be -- should have his diet restricted or -- or should maybe not restrict it, but should limit on his own the amount of fat that he -- that he takes in and someone who's going to be like Winston Churchill and eat whatever he wants and live to a ripe, old age?

A. Well, in a prospective sense, we don't have the ability to do that right now. We do that retrospectively. When you encounter 90 or 95 or 85 years of age who's been able to do whatever they wanted never with a serious medical problem, obviously they've got the right genes. And we're

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trying to identify what those right genes are in our research work and what the wrong genes are. With that kind of information, one will be able to say a lot more prospectively from in utero to the grave. But, obviously, there are patients in whom one becomes pretty rigid about that -- the recommendations. Somebody with a heart attack, somebody with a threatened heart attack or stroke, somebody with peripheral vascular disease, somebody with a strong genetic risk of heart disease, somebody who smokes heavily who won't stop. These are among those patients in whom one would really try very hard to control the cholesterol and LDL.

Q. What -- what do you tell patients who don't have heart disease about what they should do regarding eating fats or eating -- eating too much if this is a young individual and you don't know whether they're going to live as long as Churchill?

A. In those who are at risk, who I believe are at risk for heart disease from one or more perspectives, I urge them to be prudent in what they eat and to follow a diet that would help control their cholesterol and LDL and -- and blood pressure. In those in whom there's no hint

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that they have an increased risk of cardiovascular disease and they're still very youthful, if their cholesterol and LDL are elevated, I remind them that there still is a need to control this giving them the best chance to avoid cardiovascular disease -- vascular disease in later years. In someone who has an excellently normal cholesterol and LDL, doesn't smoke, still youthful, has no other obvious risk factor for cardiovascular disease who's got a moderately elevated cholesterol or LDL, I would probably leave them alone except to say to them "I think it would be best if you paid a little more attention to this." As they began to get older, I'd become more insistent on it.

Q. Now, Churchill smoked, didn't he?

A. Yeah.

Q. And many people --

A. Cigars. Cigars.

Q. Many people do smoke and live to a ripe, old age, correct?

A. I -- I don't know about "many people," Mr. Cornfeld. We'd have to know the total denominator that smoked to know a percentage that lived to old age and percentage that don't.

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Q. Have you --
A. Some of those that lived to older ages don't do so so happily. They do so with the ravages of having smoked --
Q. Have you made a --
A. -- unable to breathe well, unable to walk because of their pro -- peripheral vascular disease. They get chest pain frequently --
Q. Do --
A. -- and so on.
Q. Are you familiar with the percentage of smokers who have symptomatic heart disease?
A. No. You and I can't even estimate that not knowing the total number of patients who smoke and then not knowing the total number of those who have heart disease at one point in time.
Q. Are you familiar with the term "relative risk"?
A. I am familiar with it, but I am not an expert with it.
Q. Can you tell me what it means?
A. It means a risk adjusted for some kind of abnormality or condition or circumstances. It's trying to express risk in relative terms that are relative in a broader context.
Q. Relative to what?

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A. Whatever the issue is.
Q. Well, if there was a relative risk for smoking, relative to what? What does the term "relative" mean?
A. Among smokers?
Q. Yes.
A. Among smokers? In some context -- whether or not the one you wish me to speak about or not, I have no idea, but in some context, relative to their actual risk of cardiovascular disease.
Q. A relative risk of smoking for cardiovascular disease, what is that relative to?
A. You -- I think you've changed the phraseology on me a little bit here.
Q. If I did, I'm not -- I'm not aware that I did, but this is what -- if you saw a term that indicated --
A. Let me just -- I don't want to interrupt you, but let me say again I'm not an expert on relative risk as the term is used by the most sophisticated statistician or epidemiologist. I'm neither epidemiologist nor statistician. I'm a poor doctor. I tried to define what relative risk would mean in the usually accepted medical jargon. And one more time, it would relate risk

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with some kind of normalization scheme relative to a condition or a state or a variable or a circumstance.

Q. Do you -- do you have any knowledge about what the relative risk for smoking and any cardiovascular disease is?

A. Among patients with coronary vasospasm, it's hard to find people who don't smoke. It's very unusual to find a patient with coronary vasospasm, that is, Prinzmetal's angina, who don't smoke. I'm not sure I've met one.

Q. That wasn't my question.

A. Well, that's the way I'm interpreting it in a medical context. Among patients with heart attacks, by far, the majority of them smoke. Now, if you wish for me to answer that in a different context, define what you mean by "relative risk" in that circumstance and I'll do my best to do it.

Q. I've seen in -- I have seen the term used that the relative risk for smoking and, for example, heart attacks is -- and then there's a certain number. I've seen it for other diseases. That's what I'm asking you about. Can you tell me what that number is?

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A. I would be -- even if I knew it, and I don't, what is published, I would be -- I would not believe what is published, so I haven't spent any time trying to memorize it because in order to answer questions about relative risk, you're -- you and I are going to have to know the entire group, the number of patients that are in that category, the absolute number, the absolute number who have heart attacks, the absolute number who smoke, the absolute number who have heart attacks who don't smoke. This requires a -- an ability to identify virtually all heart attacks among a certain population.

Q. Are you -- are you aware of whether --

A. And that's very hard to do.

Q. Are you aware of whether in any groups of people anyone has determined a relative risk for smoking and any kind of heart disease such as heart attacks?

A. I'm certain that you would find from epidemiologists, from some of the demographic variables and epidemiological studies that have been done an assumed, an estimated -- estimated would be the right word -- relative risk, and I would have misgivings about it unless I could be

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assured that whoever cal -- whoever estimated that knew the total population of patients involved with the variables of interest, and I don't believe they do.

Q. All right. The same question for other risk factors: Would your answer be the same --

A. Yes.

Q. -- if I ask you about the relative risk for hyperlipidemia --

A. Yeah.

Q. -- for -- for hypertension --

A. My answer --

Q. Excuse me. Or any of the others?

A. I'm sorry. Yes, sir. My answer would be the same, yeah.

Q. I apologize. I know you know what -- what I'm asking, but the court reporter has to be able to take down the question. Not everybody who reads the transcript will be able to anticipate what I was asking. If you had a population -- well, strike that.

If you had an individual, a patient who comes in with a heart attack, do you ever try to determine what caused his heart attack or what caused his -- his atherosclerosis or what caused

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whatever other cardiovascular disease that individual has?

A. I always try to determine that.

Q. Is there a way to determine in an individual what caused a heart attack?

A. Well, there's a way to identify whether they have some of the risk factors that we've talked about, one or more, and to try to correct those.

Q. Sure. Sure. Of course. And -- and -- and as far as the risk factors are concerned, when you identify that in your patients, I -- I assume you're not -- don't just tell them "stop smoking," but if they have -- if they're overweight, you tell them to lose weight. If they don't exercise, you tell them to exercise. If they're -- if they have hypertension, you treat the hypertension and so forth; is that right?

A. That's correct.

Q. All right. But is there -- strike that.

Not everybody who has high cholesterol gets a heart attack, correct?

A. That's correct.

Q. So, you could have high cholesterol and get a heart attack for some other reason other than

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your cholesterol, correct?

A. You can, but if you have a high cholesterol and smoke, your risk of developing a heart attack is considerably higher.

Q. Sure. Do you know what that risk is compared to somebody who does not have high -- high cholesterol and smokes?

A. Again, in an epidemiological study expressed in relative risk?

Q. Relative --

A. Is that what you want me to do?

Q. Expressed in relative risk or in any other term. I'm not limiting it to that. I mean, maybe it could be, you know, 10 percent higher or 5 percent higher or 50 percent higher or what?

A. I'll have to -- okay. I will have to answer it in this way: In general, there is an -- an additive effect for the most important risk factors, one to another, so that a high cholesterol becomes more dangerous if one smokes, it becomes more dangerous if one has hypertension, it becomes more dangerous if one is a diabetic. And there is a multiplying effect of risk factors. There's no question about that. And it's significant. It's statistically

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significant. In terms of percentages of what kind of magnified risk one gets, it's probably going to vary among different populations. And it will depend a little, almost certainly, on how long one has had one or more of those conditions. If I've smoked for a day, I'm not at the same risk as if I've smoked for 40 years, 30 years, 20 years. If I've had a high cholesterol for one month, I'm not at the same risk as I am at 50 years. So -- so, all those things would have to be taken into account, but the premise that one can state with certainty, the fact that one can state with certainty, is there's an additive effect for the most important of those risk factors as one adds one to another, and that includes smoking and high cholesterol.

Q. All right.

A. And if you want to see the numbers that are available, I actually have a graph of that, not that I made, but that's been made by others and we can make it available to you.

Q. What -- what is that graph?

A. It's a graph that shows risk of cardiovascular disease per a certain number of patients who have high cholesterols, variable cholesterols, but in

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increasing amount. When one superimposes smoking or high blood pressure or diabetes, so on, how much the risk of cardiovascular disease is increased in a certain patient subset. This doesn't presume to know the total denominator. It's a certain number of individuals that exist. And if you want that, we can get it to you.

Q. Who -- who created that?

A. Well, let me see. Where -- I'll tell you where it is. It's in another book that I've edited. It's called -- let's see. Cardiovascular Trials, Clinical Cardiovascular Trials. Just been out a year. It's under the section on lipids and it's in the first few pages of that chapter. This is published by Churchill Livingston. It has a 1996 publication date. And it's a graph that is published elsewhere which I have included in that work and the reference will be there. Let me make sure of the book exactly. It's this book right here (indicating).

Q. You've pointed me to a reference in your curriculum vitae to Patel, Cohn and Willerson, The Handbook of Cardiovascular Clinical Trials. That's textbook No. 10 on your list on page 12 of your curriculum vitae; is that right?

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A. That's right.
Q. Okay.
A. In this section under lipid disorders or lipid abnormalities.
Q. All right. In any individual if you -- if you wanted to even estimate what caused that individual's cardiovascular disease, you'd need to know the various risk factors in that individual; is that right?
A. If you wanted to know the thing -- the risk factors, the factors that likely contributed to the cardiovascular disease, you'd have to know what they are, yes.
Q. If you -- if you knew that an individual -- say you had a patient who was a 60-year-old man, overweight, sedentary life-style, smokes, has hypertension, has elevated cholesterol and LDL and low HDL and has a genetic background of heart disease, that individual's heart disease could have been caused by all of the risk factors he has or some of them; is that right?
A. Yes, that is correct.
Q. All right. Any of those risk factors could have -- combined, any of those risk factors, even though they were present, may not have

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contributed; is that right?

A. Of the major risk factors and from the list you just referred to that we created earlier, I believe everything you mentioned was a major risk factor. One would have to believe that each one of those likely had some influence on the development of cardiovascular disease. In an individual patient, it would be hard to prove that. So, when you say to me that some may have contributed or all may have contributed, it would be absolutely hard to know in one individual. That would be a true statement.

Q. All right. And, Doctor, if you had a population of people who had heart disease, is there any way to determine in that population how much of the total heart disease was caused by any particular risk factor?

A. It's -- yes. There are ways at least to estimate it. It's easiest, of course, if you take a group of patients who don't have ten risk factors operative at one time. If you take a group of patients who have one risk factor or maybe two and you correct that one or two and you observe the impact in comparison to similar patients who continue to have that risk factor operative, that

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would be one way to identify the importance of a risk factor. And those kinds of studies have been done and similarly studies have been done where all risk factors were corrected as best one could in a group of patients who had multiple risk factors.

Q. Suppose you had --

A. What generally -- excuse me one second.

Q. Okay.

A. What generally has been shown is that if one corrects one risk factor, like smoking, there is a period of smoking cessation, particularly if it comes after not a terribly long period of smoking usage, but sometimes even if it is after a long period of smoking usage, the majority of the studies that have been done have shown a diminished risk for cardiovascular disease, vascular disease, heart attacks specifically and sudden death and peripheral vascular disease progression in those who stopped smoking compared to those who continued, men and women included. The same thing --

Q. Doctor --

A. I'm not quite through.

Q. I'm not --

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A. Don't I get to answer my question?
Q. I don't think that was really my question.
A. Well, I'm -- I'm -- I thought it -- I honestly thought it was. You asked me how one could prove the relative importance of a risk factor in a patient or a group of patients -- this time it was a population of patients -- who had multiple risk factors. And I said the way that's been done is to try to take such a group of patients who have only one or two risk factors and estimate its impact on the cardiovascular disease. This would be in your relative risk assessment. And as the -- as that risk is corrected and to follow these patients for a period of time in comparison to those in whom it's not corrected because they won't allow it to be corrected or historical control and then determine what the impact is. That's been done. That's been done in numerous studies and the results are the ones that I said.
Q. Okay. I --
A. Similarly, if one corrects multiple risk factors -- this, you're interested in, I know. If one corrects multiple risk factors, one can show an important beneficial effect in the

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prevention or attenuation or delay of progression of cardiovascular disease.

Q. All right. I appreciate that. I -- I really don't think that was what I at least meant to ask --

A. Well, I was trying.

Q. -- in my last question, but --

A. I was trying.

Q. -- I understand. Let me -- let me ask this regarding what -- what you just said and then I think we have to break because we're out of tape. The -- the studies that you're aware of where -- where risk factors have been corrected, are you aware of any randomized studies in that regard?

A. It's hard to do a randomized study.

Q. Are you aware of any?

A. No -- no, sir, I'm not. It's -- but I want to add that's what one would like to do to be sure.

Q. Okay.

A. It's hard to do because you have to have a population willing to be manipulated in that manner. And there are many people who smoke -- if that's what we're talking about -- or follow some diet that they're not willing to change. Or

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if they say they're willing to change, they don't or can't. So, conducting a randomized study, very, very difficult to do. Also, as regards some of the risk factors -- and this includes smoking and cholesterol today -- I don't think physicians, certainly the leaders of cardiovascular medicine, would be very willing to allow people to remain with very elevated cholesterols or LDLs or to smoke if they could prevent that. That is, they themselves would not be willing to engage in randomized studies. I'm certain that there's an adverse effect from both smoking and elevated cholesterols.

Q. Are you aware of with respect to the studies that have looked at the effect of smoking cessation, whether in those studies anyone looked to see whether those people who stopped smoking also improved other life-style factors such as diet or exercise?

A. There are many different studies. In some, multiple risk factors were corrected. In others, there was an attempt to maintain other things very constant or -- let me reword it. I'm sorry. In other studies, there was an attempt to evaluate just one or two risk factors. This is

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what I said a minute ago. They tried to identify a population of patients who were not profoundly hyperlipidemic or followed a sedentary life-style or so on so that they really could observe the impact of stopping smoking.

MR. CORNFELD: Do I have any more time?

Q. (BY MR. CORNFELD) All right. When we come back, I will ask you to identify those studies for me so --

A. Well, I --

Q. But we need -- we need to break now because we're out of tape.

A. Okay.

Q. So, whatever you're going to say, you better save it.

THE VIDEOGRAPHER: The time is 4:07 p.m. We're going off the record.

(Short recess.)

THE VIDEOGRAPHER: The time is 4:19 p.m. We're on the record.

Q. (BY MR. CORNFELD) Doctor, when we broke a few minutes ago, I was -- I told you I was going to

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ask for you to identify for me any studies you're aware of that looked at the effect of smoking cessation, and you were kind enough to -- to take a look during the break we -- we just had. Have you located them?

A. Well, I -- I mentioned to you during the break that I think the Framingham study will be one of the best sources of this kind of information, so I was trying to check to be sure that was true or not. In my book, Cardiovascular Medicine, your Exhibit 2, Willerson Exhibit 2, on page 1820 and in table 24-11, there is some support for the statements that I have made to you that cessation of cigarette smoking is associated with a marked reduction in risk of cardiovascular disease that approximates that in nonsmokers and that this -- the Framingham work suggests that this is independent of other associated risk factors, but even greater when they are present.

Q. Were you referring to a portion of the text?

A. Yes.

Q. And which portion is that?

A. And that's under "Smoking" on the right-hand side of that page. It is page 1820, the first paragraph, and then the table below, 24-11.

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There are many studies of smoking cessation and a number of them are going to be referenced in manuscripts that I've already identified for the State of Texas lawyers that are now in your possession and I think you'll find other work there, but it is this Framingham study that probably would provide the greatest insight. And I had said to you also during the break and to some of the other lawyers here that discussions with Dr. Kannel and Dr. Castelli, leading investigators in the Framingham study, would probably be very useful in addressing the issues you've posed to me.

Q. To see whether they have data that would --

A. To allow them to make available to the Court information about this specific question.

Q. The question being the effect of smoking cessation in people who did not also improve other life-style risk factors such as exercise or diet or other factors; is that right?

A. Or -- it is or did not have marked abnormalities that would identify other major risk factors as being operative.

Q. All right. Doctor, let me ask you about what I at least intended to ask when you -- when you

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discussed the -- the studies on smoking cessation. And I appreciate the discussion because I certainly plan to get into that as well, but what I -- what I thought I was asking or intended to ask was if you had a population of, say, all of the people with heart disease in the City of Houston or all the people with heart attacks in the State of Texas or all the poor people or all the rich people, just a population like that and you had just a group of people in that group that had heart attacks, is there any way to determine how much of the disease was caused by -- in that group was caused by the different risk factors?

A. One would have to go through each individual in that group and identify the frequency of each of the risk factors. And from that, one could estimate the impact that single and multiple risk factors had. You know, this -- there is one other evident problem with this kind of analysis and, that is, that one presupposes one knows all the risk factors. And to be honest about it, I doubt if we do.

Q. All right.

A. So, calculations of percentages in the absence of

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knowing all risk factors is the same kind of problem as not knowing everybody with a certain trait.

Q. Okay. Let's -- let's assume, just for the sake of this discussion, that we know all the risk factors.

A. All right.

Q. And let's say we wanted to try to find out how much heart -- how much of the heart attacks in all the poor people in the State of Texas were caused by smoking, how much were caused by elevated LDL, elevated cholesterol, hypertension, diabetes, genetic factors, age, cocaine abuse and the various other factors that you mentioned. The first thing I guess one would have to do, based on what you said, is you'd have to find out the prevalence of the various risk factors in that population; is that right?

A. Right.

Q. So, you have to find out how many poor people in the State of Texas smoke cigarettes; is that right?

A. Yes.

Q. Would you have to find out how much they smoked?

A. It is a number of cigarettes smoked. In many

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studies, it seems to be the major factor and in some, it's a duration and the number. So, I think I -- just to be as comprehensive as possible, I'd want to know both, numbers and duration.

Q. All right. You would also have to know how many of those people had elevated cholesterol and how elevated it was; is that right?

A. Yes.

Q. And the -- and -- and how many of them had other aspects of hyperlipidemia or lipid disorders --

A. Right.

Q. -- such as elevated LDL or decreased HDL; is that right?

A. Yes.

Q. And the same thing with the prevalence of the other risk factors in that population?

A. Yes.

Q. All right. Because -- and you'd have to know each of those in order to determine -- for example, you'd have to know the frequency of cholesterol elevations to determine the contribution of all of the risk factors; isn't that right?

A. You know, I -- I -- I think we're just saying the

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same thing.

Q. All right.

A. And, that is, that to try to estimate the importance of single or multiple risk factors, we have to know their prevalence in a certain population.

Q. Of all of the risk factors?

A. I'm -- I'm in agreement with that, yes.

Q. Okay.

A. I -- I do --

Q. Do you know --

A. I do want to remind you in this regard, though.

Q. What?

A. That the Framingham study concluded that smoking is the major modifiable risk factor --

Q. I -- I saw that.

A. -- at least in the Framingham population. I would be skeptical that it would be terribly different in the poor or the rich or the oil men or the ranchers in Texas.

Q. Or Texans or people from Massachusetts?

A. Right.

Q. My -- my question, though, is not which are the most important or which of the major ones, but how -- to put a number, to put a quantity on it,

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how much of the heart disease was caused by any particular factor?

A. These would be estimates, at best.

Q. Okay.

A. But one would need the information we agreed on --

Q. All right.

A. -- to try.

Q. Are you aware of any studies in Texas looking at the prevalence of different risk factors; in other words, how many Texans or specific groups within Texas have hyperlipidemia or hypertension or how many of them smoke or anything like that?

A. I mentioned the study among the Latin American population with -- particularly with diabetics on the Gulf Coast. So, that's one specific set of studies that has made -- attempted to make that evaluation. I'm not aware, I'm not personally aware of other studies of other populations in Texas relative to these points. I would imagine that in Austin that the Government and maybe the Commissioner of Insurance has some information about specific demographic groups in Texas. How accurate or complete that would be, I have no idea.

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Q. Okay.

(Willerson Exhibit No. 17 was marked for identification by the reporter and is attached hereto.)

Q. (BY MR. CORNFELD) Doctor, let me hand you what's been marked as Willerson Exhibit 17. You earlier mentioned that there was another collection of literature that had been compiled with respect to your opinions other than the articles that we went through earlier today.

A. Yes.

Q. And I believe that what I'm going to hand you contains that literature. This is a letter that was sent to you on August 15, 1997 by Harriett Chaney that has attached to it various -- various articles and excerpts from your book. Some of this is duplicative of what we went through earlier, but some of it is not. But would you confirm that this is a letter and various other materials that were sent to you on or about August 15, 1997?

A. I believe that it is and it's a result of Dr. Chaney copying some manuscripts that I had

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made she and her associate aware of that were in support of my convictions about smoking and risk of cardiovascular disease.

Q. All right.

A. Some of it is duplicative and some of it is not.

Q. All right. There's also attached to the letter -- actually immediately behind the letter is another copy of Exhibit 16, that list of journals with pages. Seeing it here, does that help you figure out what -- what that page was meant to include?

A. Possibly it relates to this additional group of manuscripts that have been copied.

Q. Actually, it didn't in any way I could figure out.

A. Did not?

Q. No, not that I could figure out anyway.

A. Then I don't know.

Q. Okay.

A. I don't know.

Q. Doctor, the letter says, "Thank you for the prompt editorial feedback on your list of opinions." What is that referring to?

A. I believe that I was sent originally a list -- I'm not sure about this. My memory is really

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hazy about this. But after our meeting, our original meeting, there was some attempt to find some of the manuscripts that I had mentioned, and I may have been sent a list of those without the copies of them and asked to say "Is this right? Is this what you meant? Or does it approximate what you meant?" And I may have said "yes" or -- or "yes, but you didn't find this" or "that" or something. And then this came thanking me for that and sending me copies of what had been put together and what would be transferred to the lawyer. I think that's what that refers to.

Q. Do you have a copy of that list still in your possession?

A. I doubt it. I don't know that I don't, but I certainly don't remember that I do.

Q. If -- if you do, I would ask that you -- that you take a quick look and see and, if so, bring it with you to the next session when we resume.

A. All right, but please don't count on it because I don't --

Q. I understand.

A. I wouldn't know where to begin to look right now.

Q. All right. If it were me, I'd ask my secretary.

A. Well, it's a little different.

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Q. All right. All right. Doctor, attached to this letter is -- is -- I mentioned is a number of articles. The -- just so the record is clear, there is also the -- the photocopies of excerpts from your book, Cardiovascular Medicine, that is another copy of what was identified earlier, but during the break, you went -- in response to my question regarding studies on smoking cessation, you went through this copy of the excerpts from your book and there are some notations on page 1820. I think two tables got checked and --

A. Actually, only one --

Q. It was stamped --

A. Actually only one table. That bottom table was what I meant to check.

Q. Oh, not the -- that's table 24-11?

A. Right.

Q. Not the -- not the top table?

A. I think the top one refers to serum lipids and the bottom one to smoking and smoking cessation. If you'll check that for me.

Q. Yeah.

A. We were talking about smoking cessation.

Q. Here. Take a look.

A. (Witness complies.) So, it's table -- yeah --

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yeah. That's correct. It's table 24-11 on page 1820 that I wanted to call your attention to. It shows risk of death by cigarette smoking status for continuing smokers and former smokers among men and women. And then in the text of that page is a paragraph that I was calling your attention to about the influence of smoking and quitting smoking on risk of cardiovascular disease.

Q. All right. In table 24-11, there are various numbers. For example, it says mortality overall for men continuing smokers is 1.8, former smokers is 1.2. Do you know what those numbers mean?

A. Well, the title says they represent the risk of death by cigarette smoking status for smokers of one package per day for 30 years in the Framingham study. So, this is a well defined population where one does know the denominator and one has characterized the patients in terms of their smoking usage and then examined a rather clear end point, mortality. And it had to do with overall mortality and what was estimated to be mortality from cardiovascular disease and what was estimated to be cancer-related mortality and then looked at risks in men and women for those who continued to smoke versus those who didn't

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and adjusted the risk based on age.

Q. Well, if we can look at the cardiovascular line for --

A. Yeah.

Q. -- continuing smokers who are men, it says 1.6. Do you know what the number, 1.6, means?

A. It's an age-adjusted risk ratio for these individuals.

Q. Okay. So, it's a ratio. Do you know what it is a ratio to or a ratio of?

A. You know, I can -- I can only read the table as you can, Mr. Cornfeld. If we need additional information about that table, I propose that we call Dr. Kannel or Castelli or both of them.

Q. All right. Well --

A. I think that would be helpful. But the comparison -- the comparison as it says in the footnote to the table is with nonsmokers. So, it's age-adjusted risk ratio and the comparison is with nonsmokers and they've got a very specific group of their -- of the individuals they followed identified, that is, people who smoked one pack a day for 30 years and they looked at mortality or not and compared it with nonsmokers, continuing smokers, former smokers,

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broken down men and women. And then it was adjusted for age. And their adjustment for age might be the thing that you and I would have to talk to Drs. Kannel and Castelli about exactly how they did that.

Q. Okay. But for -- for example, just the -- the 1.6, would we also have to talk to Drs. Kannel or Castelli to find out what that 1.6 --

A. I thought we -- I thought I just --

Q. Okay. It's a --

A. -- told you.

Q. It's a ratio of what to what?

A. It's a ratio of current smokers to nonsmokers.

Q. Current smokers of what?

A. Based on their risk of dying.

Q. Okay.

A. Age-adjusted current smokers, a pack a day for 30 years versus nonsmokers. I think that's clear.

Q. All right. The -- the risk of dying, would that be a -- the -- the relative risk we talked about earlier?

A. I think they -- I don't think there's too much relative about being dead or not.

Q. Well, the risk, we're talking about; the risk, not the dead.

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A. Well, but that -- this is where the ratio comes in in terms of the total number of individuals they have and the smokers and nonsmokers. They can calculate a -- a risk ratio from that.

Q. Do you -- do you have any understanding of how they do that, what the calculation is?

A. I'm not sure how they adjust it for age. I think the rest of it is -- is understandable.

Q. Okay. Well, explain it to me.

A. I've tried. What else can I do?

Q. Maybe I'm just too dumb. I mean, what --

A. No.

Q. I mean, a ratio is a number of one thing to another like --

A. It's the number of smokers to nonsmokers. Smokers to nonsmokers.

Q. All right. Smokers to nonsmokers --

A. Who died.

Q. -- who died. All right.

A. And it's -- and it's specific characteristics of the smokers. It's not all smokers.

Q. You mean -- you mean continuing smokers or former smokers of --

A. Yeah.

Q. -- one pack a day?

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A. Yeah.
Q. For 30 years?
A. Yeah.
Q. There's nothing on that table that indicates whether any of these comparisons are statistically significant, is there?
A. There are no P values on that.
Q. So, we don't know whether this is statistically significant?
A. Well, I'm sure we -- I'm sure we can find out easily enough.
Q. Oh, I'm sure we could too, but it's just not in the -- not on the page, correct?
A. Let's look at the text above it. Certainly their interpretation of it is these are biologically important risks. And these are two of the most highly regarded epidemiologists in the world.
Q. I -- I understand that, but -- but neither the text nor the table indicates which, if any, of these comparisons is statistically significant, correct?
A. They do not.
Q. All right. And if they are statistically significant, to what level?
A. Right.

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Q. What level do you regard as statistically significant?

A. Well, it depends on the statistical comparison and what kind of T test -- I'm sorry, what kind of assumption is made about the level of statistical significance, but in general, a P less than .05 is statistically significant. There are different kinds of T-tests that are used, two tail, one tail, some -- some corrections made for a variety of other things so that sometimes a stricter interpretation is required of significance, a lesser P value. But generally a P less than .05.

Q. All right.

A. I suspect those would be statistically significant. I'd be surprised if they're not.

Q. Does it -- does the text indicate from where this table came?

A. Well, it comes from the Framingham study, but exactly what -- what publication, I'm not -- not sure.

Q. If we were to look at the original, we probably could determine whether any of these or, if so, which ones of these comparisons in table 24-11 on page 1820 of your book is statistically

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significant?

A. That should be true. Returning to the original publication, one should be able to do that or a discussion with Castelli and Kannel.

Q. All right. Doctor, let me hand you back -- or you have it there, don't you, Exhibit 17?

A. I have it.

Q. All right. Earlier today, I asked you to point me to the studies that were brought to the deposition that provided the basis for saying that smoking injures the vascular endothelium. I'd like you now to tell me if there are any additional papers that are part of Exhibit 17 -- the ones that are duplicated, you don't have to tell me again, but any additional papers that are in that exhibit that provide a basis for that statement.

A. No. I really would have to spend the time looking through them to see. I'm certain there are some.

Q. All right.

A. Because this came from a group of papers that I indicated would be supportive of those concepts and today we've identified some more of them. I have given you the names of some other authors

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and approximate publications that would also be supportive of the position that I've taken, but, you know, I -- I have not looked through these pre -- prior to coming here. I had glanced at this group of manuscripts when Dr. Chaney sent them to me to be sure that in general they were what I had mentioned, but I haven't made any effort to try to create a list or read something specific for our discussion today. So, it would take a little bit of time to do that, but I think what I've already given you from the other list would be very helpful to you. It also would allow you to look among these papers and find the support for the positions that I've taken. And there are other manuscripts, as I mentioned. So, there are so many that are supportive of this position that if we were to try to make a list of even most of the major ones, it would take quite a time, but you have some of them.

Q. Maybe before we finish, we'll have time to ask you to go through Exhibit 17.

A. All right.

Q. But I -- I want to -- I also would like to catch up on something else and, that is, you told me another one of the opinions that you expressed in

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that meeting with the attorneys and that you have today regarding smoking is that there is substantial evidence to show that smoking affects serum lipids by reducing HDL, either frank smoking or passive smoking.

A. Uh-huh.

Q. Can you tell me what studies support that -- that statement?

A. Again, there are -- there are -- there are several. And there's one in a recent -- in an upcoming issue of Circulation or a paper just published in Circulation in which passive smoking is shown to reduce HDL levels in children, children living in households where one or both parents smoke. I believe this has just been published in Circulation. It got some national attention in the news media. So, it would be within the last month. And I don't remember the authors of it, but Circulation 1997, September -- August or September. It's not the only evidence that smoking affects HDL levels in this -- in my book, Cardiovascular Medicine, on this infamous page --

Q. Are you back on 1820?

A. Uh-huh.

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Q. All right.

A. You will remember this page now, Mr. Cornfeld.

Q. That's right.

A. On page 1820, moderate exercise was found -- I'm reading from the page on the left-hand side in the second paragraph. "Moderate exercise was found to have a protective effect against coronary artery disease in young and old men in the Framingham cohort at any level of other risk factors. It is clearly useful as an adjunct to a comprehensive risk reduction program because it raises HDL cholesterol, helps to lower blood pressure, improves glucose intolerance, and helps to control obesity. Cigarette smoking was shown to be a powerful risk factor for atherosclerotic cardiovascular disease" in the Framingham study. "This is not unexpected, since smoking lowers HDL cholesterol, raises fibrinogen, aggregates platelets" -- this is one of the things I mentioned earlier -- "decreases the oxygen-carrying capacity of the blood, and causes release of catecholamines, making the myocardium more irritable." I'm pretty sure this is from John Oates' chapter in this book.

Q. All right. And --

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A. Yeah. Well, or the chapter right before it, actually.
Q. I -- I -- I beg your pardon?
A. Or the chapter right before it.
Q. Right before John Oates' chapter?
A. Uh-huh.
Q. This is --
A. My book, Cardiovascular Medicine.
Q. Right. But he cites -- the author of this chapter refers to reference No. 22 for support for this and that is a publication by Flay, F-l-a-y, et al., entitled "Smoking Epidemiology Cessation and Prevention" from CHEST, Volume 102 in the supplement, 1992; is that right?
A. Yes.
Q. Do you know that study?
A. I'm certain I've seen it. I don't recall all the details of it just offhand.
Q. Can you recall anything about it at this point?
A. Well, that it's supportive of the statement that's made here.
Q. Do you -- do you -- do you know what population they looked at?
A. I don't remember.
Q. All right. Is there anything else in the

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materials that you have that supports the position on --

A. I'm sure --

Q. -- smoking and lipids?

A. Yeah. I'm sure there is, but I would have to look through to tell you exactly what -- which ones. And I'm certain that that manuscript in Circulation recently, the reference list, will have a number of publications that deal with the influence of smoking on lipids, passive and real smoking.

Q. What about the effect -- the effect of smoking on LDL or VLDL? Is there any literature you're aware of that indicates that there are such effects?

A. Uh-huh.

Q. What -- what is that?

A. Well, some of it again will be in material that we've given you and I'll have to look for the specific references, but the general finding has been that smoking elevates both of them, LDL and VLDL, while lowering HDL.

Q. Can you -- can you tell me studies -- what studies you have in mind?

A. We've given you a body of references.

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Q. So, somewhere in there?

A. That will be -- that will include all of the points that I've made. And I'll have to look and give you specific references for it. I will try to do that for you.

Q. Are you -- are you aware of any literature that was -- or studies that were supported or sponsored by the -- the tobacco industry or any companies in the tobacco industry on smoking and the cardiovascular system?

A. In general, I know the tobacco industry has supported research for -- related to smoking and a variety of different kinds of physiological abnormalities, and I think some of it includes work in the cardiovascular system, but I -- you know, I have not been supportive myself in that way nor has anyone who works with me directly. I though am aware from colleagues around the country that they have received support from the tobacco industry for various kinds of research, including some related to the cardiovascular system.

Q. Are you aware of any -- any publications by the -- the -- that were supported by the tobacco industry --

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A. There would -- there would --
Q. -- just beyond smoking and heart disease?
A. There would be -- certainly be some studies in which a footnote says that this was supported, in part, by a grant from some tobacco company. That's not something I look for regularly in the things that are published. I don't try to find out who supported the -- the work. That's always buried in a footnote and you'd have to have a real preoccupation with that to know.
Q. So, what -- what I'm -- what I'm trying to get at is whether you're going to say, "This study is" -- "should be disregarded because it was supported by the tobacco industry" or "I know that study was a great one because it was supported by the tobacco industry" or anything like that.
A. No. I have no intention of doing that.
Q. All right. And -- and -- because that's not anything that you look at --
A. No.
Q. -- is that right? And so I take it that any statements that you've seen in the literature or any -- any studies, any even comments or reviews, whether that was something that was financially

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supported by the tobacco industry is something you're not even aware of; is that right?

A. It's something I paid no attention to. I mean, I -- I try to look at studies not by whose -- who it was supported by, but what the facts are and what the evidence is and how well supported it is. In general, I care much less who supported the study. I start with the assumption they've been done honestly.

Q. Okay.

A. If I were to be critical of the study, it would be on different grounds, not who supported it.

Q. Do you believe that you know the mechanism by which smoking exerts its effect on the vascular system?

A. Well, I know some of the mechanisms. I -- I know that its influence to cause vasoconstriction or spasm is very unfavorable, reduces blood flow. In a patient with coronary disease, it's very unfavorable to have the heart rate increased and heart rate and blood pressure increased because this requires a higher oxygen delivery to the heart and the narrowed coronary artery can't do that, can't provide it. I know that the influence of smoking to cause aggregation of

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platelets is a very unfavorable thing since that's the initiation of a thrombus. And then the physiologic information that smoking injures endothelial function leading to thrombosis and vasoconstriction, fibroproliferation, those are very unfavorable things. An important reduction in HDL would also be very unfavorable because that's a lipoprotein that is protective against progressive atherogenesis.

Q. When did -- when did medical science learn of the importance of HDL?

A. There's been a presumed importance of it over the last 10 years, at least, 10 to 15. The best evidence that it is very important, in my opinion, has become available in the last seven or eight years.

Q. So, prior to that time whether smoking caused a decrease in HDL would not have been regarded as particularly important; is that right?

A. Well, it would have -- it would have met with a variable response, I think. There would have been some who would have been worried about that, others who would not have been as worried. And then as the evidence has developed that HDL is important in and of itself as a risk factor and

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evidence that even the administration of HDL can be protective in certain animal models, a conviction has developed, I would say in the last seven to ten years, of the absolute importance of HDL. So, it probably wouldn't be totally fair to say that any information about HDL 20 years ago would have been considered as trivial, but it would be fair to say that it would have been at least controversial 20 years ago.

Q. All right. How does smoking cause vasoconstriction?

A. Well, it -- I'm not certain we know all of the ways that it does that, but it probably does it, in part, through its influence on platelet aggregation and the release from the aggregating platelets of substances that constrict arteries, notably Thromboxane A2. It probably also influences it through the -- when I say "probably," this is what would be suggested by available information from studies. Probably also does it as a result of some activation of the sympathetic nervous system and -- and predominantly the alpha-adrenergic portion of the sympathetic nervous system. I wonder if it -- well, my wondering won't matter to you much, but

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I wonder if it doesn't cause a release of endothelin from damaged vessels. Endothelin is a very potent vasoconstrictor which is present in the endothelium which is released with endothelium injury, and my bet would be beyond what I just mentioned to you is there's evidence for -- that endothelin may be a factor too. We haven't had antagonist of endothelin until recently.

Q. All right.

A. So, we should know about that pretty soon.

Q. Now, you -- you said one of the -- you believe that one of the mechanisms through which smoking causes vasoconstriction is by causing aggregation of platelets?

A. Uh-huh, and the release of platelet-derived mediators that cause vasoconstriction --

Q. Is that a --

A. -- of which Thromboxane, t-h-r-o-m-b-o-x-a-n-e, A2 would be one notable example.

Q. Are the -- is the release of these mediators a consequence of the platelet aggregation?

A. Yes, sir, it is.

Q. All right. And how does smoking cause aggregation of platelets?

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A. Again, we may not know all the ways that it does that, but probably, in part, by stimulating alpha-adrenergic receptors that are on platelets.

Q. Stimulating alpha what?

A. Adrenergic, a-d-r-e-n-e-r-g-i-c, receptors that are on platelets. When you stimulate those receptors, the platelets aggregate.

Q. What is it in smoke, in cigarette smoke, that does that?

A. I don't think anyone knows for sure. The nicotine has been incriminated, but other studies have suggested that it may be other constituents of tobacco or tobacco smoke.

Q. What are those other constituents?

A. I don't know all of them.

Q. Can you tell me about any of them that would do this or have been proposed to do this?

A. That I could provide proof for, no. Nicotine, there would be evidence incriminating nicotine, but some studies have suggested that it may be broader than that.

Q. Have they suggested what those other --

A. No.

Q. -- components are?

A. No. Just these would be some studies that would

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show that nicotine alone may not be able to explain the magnitude of the effect.

Q. How does smoking increase the heart rate?

A. Probably by its influence on the adrenergic system that I've mentioned now several times and by the -- causing the release of catecholamines c-a-t-e-c-h-o-l-a-m-i-n-e-s, which themselves promote increases in heart rate and blood pressure.

Q. What component of smoking does this?

A. In part, nicotine, but that may not be the total story.

Q. Have there been studies looking just at nicotine to see whether nicotine will have the effect of stimulating the alpha-adrenergic receptors or have the effect of releasing catecholamines?

A. There have been attempts to discern among the two and the results would be what I've said, that it certainly would appear that the catecholamine releases an activation of the adrenergic system is the mediator of the -- of the heart rate/blood pressure change. But what you're really asking me is: Is it just the nicotine in the smoke that stimulates that -- those alterations, and my answer is I think the weight of evidence suggests

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that nicotine is at least a contributor.

Q. Okay. But what I mean is have there been studies where they would give somebody nicotine just by itself or an animal nicotine by itself and see whether it results in the release of catecholamines?

A. Yeah. There are -- there are such studies and they are, at least some of them, associated with increases in heart rate and blood pressure that appears to be related to -- at least temporally related to changes in catecholamines and activation of the adrenergic system.

Q. Do -- who -- who did those studies? When did they do them?

A. Why -- why could I predict that would be the next question?

Q. You can go ahead and ask the questions as well as answer them, if you'd like.

A. I'd have to find them for you, okay? I'm aware of them.

Q. All right.

A. But this is not something that I concentrated on recently and I'd have to find them. They're -- they're available.

Q. Do you know how far back that that those studies

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have gone?

A. It would be studies done over the last 20 years, something like that. Maybe 25 years.

Q. How does smoking injure the endothelial function?

A. I have to answer it the same way. The evidence would be suggested that nicotine itself plays some role in that. It is certainly -- and it -- and it may be that the increase in catecholamines that occur with smoking play some role in the injury to the endothelium. Increases in catecholamines do injure the endothelium and even heart muscle cells themselves when -- when catecholamines are released in excess. And there may still be other components of cigarette smoke that play a role in this not yet identified.

Q. Are you aware of any other mechanism that might explain the injury to the endothelium besides --

A. Well --

Q. -- the release of catecholamines?

A. Okay. And nicotine itself directly. One other perspective is that the vasoconstriction and sometimes spasm associated with the smoking can injure the endothelium itself. When an artery constricts down like this (indicating) or constricts repetitively, the inner lining of the

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artery is injured. And there's some evidence for that. Where is it? I'd have to look.

Q. All right. How -- how would nicotine directly injure the endothelium?

A. I don't know how it does that. I don't think anybody does.

Q. Doctor, where do your -- your patients come from?

A. Throughout the country and, in fact, throughout the world.

Q. What percentage of your patients come from Texas?

A. The majority of them.

Q. How would -- how big a majority?

A. An estimate would be 75 percent of them, 70 to 75 percent.

Q. The -- the patients that come from Texas, is any portion of those -- are any portion of those Medicaid recipients?

A. Sure.

Q. What -- what percentage is that?

A. I really don't know. I see everybody who comes. I don't pay much attention to that. I -- in addition to making rounds at Hermann, I also make rounds at LBJ. It's a city/county hospital where everybody is indigent. I do that once a week every -- they're even below Medicaid. They don't

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have anything. So, I see the very poor and I see the very rich --

Q. Have you ever --

A. -- and everything in between.

Q. Have you ever made any attempt to determine whether your Medicaid patients are similar or different from your non-Medicaid patients?

A. As regards what?

Q. As regards to anything. As regards to the diseases they have, their risk factors, their willing to comply with your advice, anything like that.

A. No. I have not made any compilation of that. I mean, there are people from all socioeconomic walks of life that are more or less willing to comply with recommendations that are made. Sometimes the poor are unable to comply with certain medications, as you would know, quickly, even unable to buy medicines let alone follow some diet or life-style. And I would say, I guess, that the very poor and uneducated are probably, as a group, more likely to be not very receptive to recommendations about stopping smoking or stopping using cocaine or other illicit drugs. And they also have a higher

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incidence of HIV-related diseases. But those are generalities and while I'm sure they're true, I don't know that there are other major differences, but among these groups of patients, they all have cardiovascular disease and none of them are immune from any kind of cardiovascular disease.

Q. Is socioeconomic class a risk factor for heart disease?

A. I think that it is and probably should have listed it earlier.

Q. In what way?

A. It's not one that's widely touted, but as one sees all of these patients, one certainly comes to learn that many of the poor and the disadvantaged and the not well educated smoke. In my experience, it's the majority of them that I see.

Q. I'm sorry. The majority of the what?

A. It's the majority of them.

Q. Who?

A. The poor, the disadvantaged, the poorly educated. An escape, I imagine, just as they drink. Many of them drink. And, as I said, the other problem is they can't afford specific kinds

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of diets or medications and an elevated cholesterol, no hope of getting a medicine that would normalize it.

Q. Does Medicaid --

A. Unless you buy it -- unless you buy it for them.

Q. Does Medicaid pay for those medications?

A. It does for some of them, but I'm talking about a spectrum of patients who don't have Medicaid. Medicaid pays for some of these things. Usually wants the generic brand no matter what's the best and --

Q. So does -- unfortunately, so does my insurance company that I pay for.

A. Yeah. I imagine it does.

Q. Yeah.

A. Mine does too. That's managed health care.

Q. Doctor --

A. They can't afford to go to doctors. Some doctors don't take Medicaid, don't see patients with Medicaid. So, there are many things that influence risk in those patients and I do think the lower socioeconomic class has a risk factor.

Q. Are the doctors that people on Medicaid see, generally speaking -- I know you see them too, but -- but generally speaking, are they of the

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same caliber that people who either can pay themselves or have insur -- their own insurance coverage can pay for?

A. I hope so. I hope so.

Q. What do you think?

A. Sometimes.

Q. Sometimes they are and sometimes they're not; is that right?

A. Uh-huh.

Q. You need to say "yes" or "no" out loud.

A. Yes.

Q. Okay. You said that the -- that poor people are sometimes less willing to stop smoking. Why is that?

A. Well, I -- I don't know all the reasons, but I think and I mentioned sometimes it's an escape from the realities, the harsh realities that they face, just as drinking is. I don't know just how this works, but I have a sense that smoking, particularly when it's addicting, is associated with some relaxation. And there are people who smoke who need a relief of certain tensions. I've seen that among individuals. After they smoke, they are more relaxed. They -- it's really a relief mechanism of some kind of pent-up

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tension, and maybe it's the addiction so that this would be the same for any addicting drug. Maybe it has some other mechanism, but -- and maybe it's an addiction, per se, but it certainly does seem to -- to be difficult to get a higher percentage of the very poor people to stop smoking than it is some of those who are more affluent and better educated.

Q. Does that include people on Medicaid as well as the people who are even below the level of Medicaid?

A. Yes.

Q. What do you --

A. It may also relate to education, of course. It may be easier to understand the risk factors -- the risk factor that smoking represents when one discusses that with someone who's a little better educated and can grasp the concepts and has a sense of what that means --

Q. What --

A. -- and harder for those who are less well educated.

Q. What do you tell people, your patients, who smoke and what do you -- what treatment do you prescribe for them in an effort to get them to

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stop smoking?

A. First of all, willpower. Willpower combined with my attempt to have them understand what the risks of smoking are, in my opinion, not only the cardiovascular ones, but the others, cancer and emphysema. And I try to describe that. On occasion, I've shown patients pictures of postmortem examples of what the lungs look like of people who smoke or what the arteries look like of people who smoke. Sometimes that has an effect. Beyond that in somebody who expresses a real desire to quit but believes they can't, certainly I, like other physicians, have Nicorette gum and Nicorette patches. I've employed the help of priests, influential family members, anything I can think of that might work, in short.

Q. What -- what percentage of the people who you recommend to stop smoking would you say do stop smoking?

A. Only a few.

Q. And that's true for the entire gamut of your patients?

A. I do better with the better educated a little more affluent people.

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Q. But it's still only a few?
A. It's more, but it's not all of them for sure. My guess is -- might be of the best educated, most affluent, maybe in 40 or 50 percent of them with intense effort over an extended period of time, one could get them to stop smoking. Whether that's permanent or not, I'm not sure, but for some period of time anyway. Of the disadvantaged group, less well educated, poor, I would say less than 20 percent stop. I really think probably less than 10 percent stop with the best effort one can make.
Q. Now, what about -- you mentioned cocaine addiction. The -- that the poor people who you see are also unable or unwilling to stop taking cocaine; is that right?
A. Uh-huh.
Q. What -- what do you do to help them get over cocaine?
A. Often, I've encountered them when they've had a heart attack or maybe sudden death and I've tried to have them understand that they -- what happened to them is a direct result of their cocaine usage and try to get them to see this is going to be recurred and they may not survive the

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next time. For some, that has a dramatic effect. For others, they're sometimes somewhat hostile, not interested, clearly are using cocaine as an escape mechanism from the realities that they face.

Q. Tell me about cocaine as a risk factor for heart disease. I know you listed it, but I didn't ask you much about it.

A. Well, it's -- it's, in fact, a lot like smoking. In fact, I often refer to it in talking to younger doctors as a far more powerful cigarette in that it causes more uniform vasospasm, frank obstruction of the lumen of the artery, complete obliteration. It also potentiates platelet aggregation leading to thrombosis and it injures the endothelium. Does the same things that smoking does, increases heart rate and blood pressure. Does the same things that smoking does only does it even more powerfully.

Q. Is -- is cocaine use something that is predominantly found in your poorer patients?

A. Not predominantly, but more frequently.

Q. More frequently than in your more prosperous patients?

A. Yes.

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Q. What -- do you have any estimate as to what percentage of your poor patients have cocaine as a risk factor?

A. That's really -- of those with heart attacks, the poor with heart attacks -- this is going to be a moving target because it would have been more frequent before all of the publicity about it. It's had some impact to reduce the usage of cocaine, but I would say maybe of the very poor with heart attacks, 20 percent of them use cocaine.

Q. And there was more earlier?

A. I think probably a little more earlier.

Q. When was that?

A. Five to ten years ago.

Q. Prior to now?

A. No. A little more, five to ten years prior to right now.

Q. Okay.

A. And a little less right now.

Q. How about earlier than ten years?

A. I don't know.

Q. Okay. Do you have any knowledge about whether there's been fraud in the Medicaid system?

A. There's alleged fraud and you and I both read

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about that.

Q. Sure.

A. I think it's more innocent than it is portrayed in newspapers, by and large. And the alleged fraud is that doctors bill for things they haven't done. You know, this can vary from the very simple error -- let me give you an example. One bills Medicare over two weeks and at a certain level for a daily charge to a patient and is supposed to write in the chart what one did on that day. Saw the patient, I found this, I did this. If a reviewer of those notes believes that what was written in the note is not commensurate with the charge, this is alleged fraud. In many instances, the doctor didn't have the time to write every single thing that was done. May not have even known he or she needed to. It may have been illegible. He may have relied on somebody else to write it, a host of things. And so it would vary from that to frank abuse on the part of some doctors where they had badly overcharged or charged for something they really didn't do and they know they didn't do it or charged for the wrong thing or saw. I believe that that is really a minority of the fraud. And most of it

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is of a much more innocent kind.

Q. How much of it is innocent or not innocent?

A. You know, I -- I said I hope and believe that most of it is of the innocent kind.

Q. Okay. Can you put a quantity on that?

A. I don't know how I would do that. I can hope. I can hope that less than five percent of it, less than two percent of it is of the malicious, criminal kind.

Q. But you're not -- you don't have --

A. How would -- how would one know for sure? How would you know?

Q. Doctor, what are the -- the cardiovascular diseases that -- I -- I don't think I asked you this. What are the cardiovascular diseases that you believe are caused by smoking?

A. Heart attacks, an entity that we call Prinzmetal's angina. I mentioned this earlier. P-r-i-n-z-m-e-t-a-l-s or vasospastic angina.

Q. That's another name for it?

A. Uh-huh. Unstable angina, progressive peripheral vascular disease. I mean atherosclerosis. Progressive coronary atherosclerosis, some instances of sudden death, particularly in the patient with coronary heart disease. And

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cerebral vascular disease and strokes.

Q. All right. Do we have the list?

A. Yes.

Q. All right. You mentioned two different kinds of angina, Prinzmetal's or vasospastic?

A. No. That's the same.

Q. Right. Right. And a second type --

A. Unstable.

Q. -- unstable?

A. Right.

Q. Is there any other type of angina?

A. There's a stable form of angina, and that relates to the presence of coronary atherosclerosis. And I think smoking is a contributor to the development of atherosclerosis. And so it's a contributor to the development of stable angina too. I just regard stable angina as almost synonymous with important coronary atherosclerosis, so I didn't mention it.

Q. All right. So, you would -- you would attribute all kinds of angina to smoking?

A. I think smoking is a contributing factor to the development of it, yeah.

Q. All right.

A. Not all by itself, but a major contributor.

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Q. How -- what else contributes?
A. Well, the things we've talked about now and quite in a bit of detail. Genetic factors.
Q. Okay.
A. Cholesterols.
Q. The -- what is the typical age range of patients who have heart attacks?
A. The typical age range is from 45 to older in men and the post-menopausal woman.
Q. Which would be what age range?
A. From late -- mid-to-late 40s and older.
Q. All right. For men, it can go from 45 all the way up?
A. For men, it can go really from -- from either one of them, it can go from age two or three years of age all the way up.
Q. I -- I mean, what's typical?
A. But typical is men, let's say, 40 and up and for women, let's say post-menopausally but 48 and up.
Q. Does it include for -- in both sexes individuals over the age of 65?
A. Sure.
Q. There are a lot of heart attack patients over that age?
A. A lot of them are in middle age, which is that

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period of 45 to 65. And then, of course, some of them are at more advanced ages, but I'd say the predominant number of infarcts are between the ages of 45 and 70.

Q. Okay. How about angina, patients who are treated for angina? What -- what ages do they have?

A. They are the same.

Q. The same. All right. How about atherosclerosis?

A. Well, that develops, as you know, in teenage years. We've learned that from some of the war casualties in teenage young men. They already had aortic atherosclerosis. So, it begins in probably from the moment of -- at the moment one can begin to eat in a western civilization, but evident, clinically evident atherosclerosis would follow these same time periods. In men, be evident generally about the age of 40 and increasing in time with aging and in women, post-menopausally and increasing with aging. And here atherogenesis or atherosclerosis relates to the atherosclerotic process involving any artery in the body so that they might have peripheral vascular disease, lower extremity disease, coronary disease, cerebrovascular disease.

Q. What I meant was not just clinically evident, but

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the age at which people are treated for it.

A. Well, that's clinically evident.

Q. Okay.

A. They're treated one way or another, either with diet or aspirin or medication to lower cholesterol, control blood pressure, every effort to get them not to smoke, exercise.

Q. You mentioned sudden death. I assume people aren't treated for that?

A. Well, they are if they're resuscitated. And today, fortunately, some are resuscitated. That's best done in Seattle where there's an emergency ambulance system that can reach patients in virtually every part of the city within three minutes, three or four minutes, with personnel trained to resuscitate people who die suddenly. And much of the patient -- sorry, much of the citizen population in Seattle has also been trained in resuscitation. This is something that's been going on there for 20 to 25 years. So, it's a model for the development of resuscitation mechanisms. We do resuscitate some people. You have to do it real fast or there's not much chance of doing it -- if you don't do it real fast, even if they're resuscitated, they're

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brain dead. So, if that's done, then one has a chance to correct certain risk factors. And there are a variety of things that are used beyond all we've talked about. They include placements today in the heart of implantable defibrillators, mechanical devices that sense a cardiac arrythmia and shock the patient, correcting it. So-called AICD, automatic implantable cardiovertor defibrillator.

Q. What -- what portion of patients in Texas are resuscitated from sudden cardiac death?

A. You'd have to know the denominator. Nobody knows the total denominator, but it's a minority. It's not a majority of them. Resuscitated so that they survive, it's a minority. It would be well under 50 percent. It probably is in the range of 10 to 30 percent would be the most honest guess.

Q. For how long has that been the case?

A. It would be the case recently. I don't know. If you went back 20 or 25 years, probably believable records weren't kept.

Q. Okay.

A. So -- but in the last five years, probably somewhere between 10 and 30 percent of patients are resuscitated. It would be community

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dependent. It would depend on the training and the -- of people and the emergency ambulance system availability and the skill of the operators and so on. We're talking about Breckenridge, Texas versus Houston where there's a Life-Flight and so on. It would be different.

Q. How -- how fast do you have to get to somebody to resuscitate them?

A. Three to five minutes.

Q. What is the typical age range of patients with cerebrovascular disease and strokes?

A. Older and -- typically older and I would say ten years later than coronary disease, something around 50 to 55 and older. You have to remember there's a lot of individual variation. There are young people who have these problems, very young, teenagers. There are many different reasons for strokes. Women, in the last trimester of pregnancy and soon after the birth of a child, are at risk for spontaneous deception, a tear in the arteries that go to the head that are in the neck, the carotid arteries. Those are young women. So, patients who have profound hypertension that's not controlled are at risk for a stroke every minute of the day and night.

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So, if someone with early onset of hypertension, if it's not controlled, could have a stroke at age 20, 25, 30. Somebody using cocaine can do that. So, there's lots -- lots of reasons. Blood clots from the heart can go to the head and occlude an artery and cause a stroke. Those are so-called embolic strokes.

Q. The -- the risk factors that you mentioned for heart disease, are those also the risk factors for strokes?

A. They are, but there's a much broader list than some of the things I'm just alluding to. The tear, the spontaneous tear in the artery, hypertension, embolic strokes, blood clots from somewhere else going to the head to occlude an artery. Even in an otherwise normal artery, all of a sudden occluded.

Q. What are the risk factors for that?

A. Underlying heart disease in which the heart is big and dilated and failing. The left atrium is enlarged. The patient has atrial fibrillation, the patient has mitral valve disease, different risk factors than for coronary disease.

Q. Are the -- are the risk factors for that type of heart disease the same as the risk factors you

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mentioned earlier?

A. No, not at all. It's -- the risk factors for mitral valve disease don't have anything to do with lipid elevations or smoking or --

Q. It doesn't have to do with smoking or it does?

A. No, not mitral valve disease. And, you know, there are many reasons for cardiac valve disease, mitral valve disease included. Rheumatic fever is one reason. Infections on the valve are another. An entity called myxomatous degeneration, which is genetic in which there's an abnormality in the structural components of the valve so that it slacks. Aging, the wear and tear of time and calcification of the valves are some of the major risk factors for valve and heart disease.

Q. Okay. Do you have any -- do you have any knowledge about -- for -- for your patients who are over the age of 65 how their medical care is paid for with a share -- if they're poor people, the share that Medicare covers and the share that Medicaid covers?

A. Some of them don't have either one. They don't have any insurance at all and they go to these city/county hospitals like LBJ. I don't know

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that St. Louis has one. But they're hospitals like Grady, like Boston City, like Cook County in Chicago, Parkland in Dallas, Ben Taub and LBJ in Houston.

Q. For patients who are on Medicaid --

A. Uh-huh.

Q. -- what portion of their care is paid for by Medicaid and what by Medicare if they're over 65?

A. I don't know for sure. I'm not certain.

Q. Do you have --

A. I think -- you know, I think in general, that that relates to outpatient care may be paid for by Medicaid and I guess Medicare too. That that relates to the in-hospital care is paid for by Medicare.

Q. All of it?

A. Not all of it.

Q. But I mean --

A. But a substantial part of it.

Q. To the exclusion of Medicaid is what I really meant.

A. I think so.

Q. All right.

A. We ought to check that, but I think so.

Q. Do you -- do you fill out death certificates?

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A. Yes.
Q. Is there a place on a death certificate to indicate smoking?
A. The part that I fill out -- I don't know the answer to that question. The part that I fill out relates to stating the cause of death, the date and time of death, major contributing factors to death and my signature. That's what the physician is asked to fill out.
Q. Would major contributing factors include, for example, smoking?
A. Well, again, it's death. It's death, per se. And most of the time, what one says is this was a heart attack or this was an instability of cardiac rhythm. This was shock. This was sepses, an infection, this was bleeding, that kind of thing. So, it's really the proximate cause of death. Not all of the risk factors that resulted in injuring the heart that led to this problem that led to death. There certainly isn't any space to do that on the death form.
Q. Okay. Are you familiar with the ICD-9 codes?
A. Are these resuscitation codes, categorizations at the hospital?
Q. No. I'm -- I'm referring to codes for different

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diseases. I think it's the international classification of diseases.

A. Okay. All right. There are so many coding systems. I guess I'm not.

Q. All right.

A. It's not something -- it's not a coding system I use.

Q. Do you have any understanding about -- I don't mean your death certificates, but death certificates in general, how accurate they are when they list the cause of death?

A. Well, I think it depends on who filled them out and how well the physician knew the patient. There are people that come to a hospital who are already dead and there's a doctor in the emergency room that pronounced them dead. And it may not be evident why they died and he or she may guess why they died. There are others who have been cared for by a doctor for some period of time. They know their medical diseases. They know they were -- why they were in the hospital. They cared for them in the hospital and they know precisely why they died. And I don't think there's much distinction of the two on a death certificate. Maybe if one could look and -- and

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try to find somebody may have said "maybe this" or "that" or the "other" or "probably this" as opposed to "absolutely this," you know, there's going to be -- it's going to depend on which patients, how many of -- which kind are you talking about.

Q. To the extent that patients don't have a regular doctor, then, would that tend to make their death certificates less accurate?

A. Probably.

Q. Do Medicaid patients tend not to have regular doctors?

A. Well, I think there's a lot of variation there. I think some of them do have regular doctors and some of them don't. How many do and don't, I would have no idea.

Q. Whether that's more or less than non-Medicaid patients?

A. I think that would really be hard to say.

Q. Okay. Have you seen any studies looking at the accuracy of death certificate information?

A. Certainly not recently I have not and have I ever? Probably in distant years gone by, but nothing recently.

Q. How many of your patients go to nursing homes?

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A. Well, it's a minority of them because even among the poor, many of their families want to take care of them. They want them to come home. If you want me to estimate a percentage of them, I would say under 10 percent.

Q. What would tend to cause one of your patients to find his or her way to a nursing home?

A. They generally don't. Somebody puts them there.

Q. What -- what are the factors that would lead to that?

A. That they're demented. That would be a main thing. They're absolutely demented and it's essentially impossible to take care of them in any other environment. Another would be that they're bedridden. They are totally incapable of caring for themselves and there is no one else or they need such a high degree of nursing care because they had some serious medical problem that they're not able to attend to themselves, like an infection that requires round-the-clock administration of antibiotics or very sophisticated medication schemes or maybe they're a diabetic and they need insulin and there's no one to give it to them, those kinds of things, but primarily demented, bedridden, unable to care

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for themselves and there is no one else who's willing or able to do it.

Q. So, one -- one or more of those factors?

A. Uh-huh.

Q. Is that right?

A. Yes.

Q. Is -- is there anything about smoking that would be -- we can call it a risk factor for winding up in a nursing home?

A. Well, it's because of end-stage disease of the lungs. It's because of lung cancer, in my opinion, so it would be debilitating diseases where one cannot care for one's self and needs the help of someone and there is no one able or willing. And I need to add to that list patients with cancers fall into this category who need frequent pain relief medication or eating, can't eat, that kind of thing. So, they would be patients with lung cancers related to cigarette use, there would be patients related -- patients with end-stage lung disease related to cigarette use and there would be patients with end-stage heart disease, multiple heart attacks with heart failure, end-stage heart failure, who would be in that category.

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Q. How common is that?
A. All of those things happen. Are you asking in my patient population?
Q. Right. And in -- and in your general experience.
A. The end-stage heart failure from smoking and multiple heart attacks among all the patients with heart attacks that I see might occur in ten percent of them, something like that. Do you understand what I'm saying?
Q. Yeah.
A. All right.
Q. You mean in ten percent of those people --
A. Of those who smoke, who have had heart attacks who then survive -- many of them die with their heart attacks, so they're no longer in this group. But of those who survive, they have multiple heart attacks and end up with heart failure, end-stage heart failure, and end up in a nursing home, it would be 10 percent or less. Of those with very severe lung disease, I'm not a lung specialist, so I'm not really the right one to ask this question.
Q. Okay.
A. And I'm not a cancer specialist either, so I'm

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not the right one to ask that, but it would be a higher percentage of patients -- in my estimate would be a higher percentage of patients who smoke who develop lung cancers or emphysema who would end up needing help.

Q. There's nothing about smoking that would tend to make a patient demented, is there?

A. Not to my knowledge.

Q. Okay. Nothing about smoking that would tend to deprive a patient of family members willing and able to take care of them, is there?

A. In most instances, not. There would be a few instances in which the family itself is very attuned to the nonsmoking business. They don't let anybody in their house that smokes so -- and they would be unwilling -- maybe they have small children. Who -- who knows all the reasons. And they would be unwilling even to have a loved parent smoke in their house. I think that would be a minority of the time.

Q. Yeah. I hope that's a distinct minority.

A. I do too.

Q. Are you aware of any racial differences on the effect of smoking on the cardiovascular system?

A. My -- my sense is that this has not been studied

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carefully enough generally. So, I'm going to be a little bit reluctant to accept that a paper that is found would necessarily prove one thing or another. I think it's something that one does need to study further. I hope not prospectively by people smoking, but retrospectively trying to examinate (sic) it further -- examine it further. I have a sense that it's been a little more disadvantageous, that it probably is more disadvantageous in the Afro-American population.

Q. Why is that?

A. It's just my guess from my own experiences. Maybe it's what I've seen. I see a substantial number of black patients who are indigent and poor who smoke and I see a lot of disease among them. And I've been impressed that smoking is a very bad thing in that population as I have generally, and it may just be my bias. I -- as I said, I -- that's my sense. That's my impression, but I have just as great an impression that this has not been studied carefully enough. Let me answer one call. I'm sorry, but afraid it might be the Bishop.

Q. Sure.

THE VIDEOGRAPHER: The time is 5:47

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p.m. We're going off the record.

(Short recess.)

THE VIDEOGRAPHER: The time is 5:55 p.m. We're on the record.

Q. (BY MR. CORNFELD) Doctor, do blacks tend to be on Medicaid disproportionately to whites?

A. Yes. I think they are.

Q. Do Hispanics?

A. Probably. Those are my guesses. I don't know the facts, but I would -- I would be fairly certain that both are true.

Q. All right. You -- you mentioned earlier a bunch of studies with acronyms or initials?

A. Uh-huh.

Q. Are you aware of a study called M-I-L-I-S?

A. MILIS, yes.

Q. MILIS. What is that?

A. It stands for interventions to limit infarct size and it is a study originated by Gene -- Eugene Braunwald out of Harvard. I helped him originate those studies. And they were the precursor to the TIMI studies, which we've talked about before.

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Q. All right. Was there a MILIS study that dealt with racial differences?

A. Yes.

Q. How many specifically?

A. This goes back a long time. It's going to be in the late 1970s. And I may even be an author on it. It's that far back. We have to look and see. But fundamentally, it tried to look at whether there were different outcomes with micro -- with micro infarction in Afro Americans versus Caucasian populations. The MILIS studies, like the TIMI studies, evaluated a certain intervention in heart attacks. This was prior to thrombolysis. So, it evaluated the number of drugs like hyaluroni-dase and glucose and insulin and a variety of things like that. It tried to look at whether the Afro-Americans have a more adverse prognosis than Caucasians post-heart attack, and it concluded that they do, that they're a different subset and that they have higher risk for heart attacks, are of higher risk from heart attacks than do -- does the Caucasian population generally. And it broke it down to individuals at different ages and men and women and I would have to look back to see exactly what

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all the subsets were. It might be in my CV. If you hand it to me, I'll tell you.

Q. Okay. You're now looking at Exhibit 1.

A. I'll listen -- yeah -- I'll listen to you if you want --

Q. No.

A. -- to keep going.

Q. No. I'll wait.

A. It utilized the city/county hospitals in the system to do the study and Parkland was one of them.

Q. Was it just one study that you're talking about?

A. Again, this was that MILIS database from which patients were used. And there may have been more than one paper about the same thing, but it was the same group. How do you know about the MILIS studies?

Q. Well, just maybe I might have done a little homework.

A. I should have mentioned it.

Q. I might have even looked at your CV.

A. It's so long ago that....

Q. 1987, Doctor.

A. For MILIS study?

Q. "Effects of Gender and Race on Prognosis After

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Myocardial Infarction."

A. Sounds like it. Boy, this is a little late in the history of the MILIS. What number is that?

Q. Actually, I don't know.

A. Okay. Well, I'm in the right year, so -- yeah. It's in the Journal of the American College of Cardiology, Volume 9473, 1987, and I am a coauthor on it.

Q. All right.

A. Not a very prominent one, but I am one.

Q. So, you participated in that study in some way?

A. Yeah. Well, they reused information that was gathered from our center and the other centers and Dr. Tofler, the first author, made the evaluations. So, as a participating member of the team, I'm listed as an author.

Q. Did you -- did you find in that study that -- and by "you," I mean your team -- that blacks had a worse prognosis following a myocardial infarction than white people did?

A. Yes. That's what I just alluded to a minute ago.

Q. Okay. And in particular, that was true for black women?

A. I believe that was the case, yeah.

Q. All right. Do you recall that you actually found

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that black women in your study smoked less than white women?

A. I -- that may well be true. I would have to look back and see whether it was. You know, you need to keep -- you need to keep in mind it's not a terribly large study. At best, this was a study of several hundred individuals, not thousands, and there was no representation that this was necessarily representative of the population at risk. I don't know where -- where your questioning is meant to take me, but I would immediately be critical of our own study on the basis of no guarantee that it's representative of anything in relatively small numbers and these are patients with heart attacks. So, this is a specific population.

Q. At least in that population if the -- if the African-American women smoked less than white women, but had a worse prognosis after myocardial infarctions, would that tend to show in that population that smoking had a -- a smaller effect in the -- in the blacks than in the whites?

A. Not necessarily for the reasons that I've mentioned and also for reasons that I mentioned earlier. This is a very specific point in time

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where one has a heart attack and multiple things going on. We talked about this a little bit earlier. One has alterations in blood pressure and heart rate and catecholamines and blood sugar and a variety of things. And the black population clearly has a higher incidence of hypertension than does the Caucasian population. So, one very important factor in prognosis in the midst of a heart attack and after relates to blood pressures. And let's just say these women had higher blood pressures -- I don't remember whether they did or not. I don't know that we even utilized it -- than the white women and they had a poorer prognosis and some other factors didn't seem to be as important. It may be that in that particular time and setting, the influence of high blood pressure is really a dominant one overriding other risks. And it would be more frequent in Afro-Americans. That's just an example of the kind of thing I've got in mind, but it's the potential correct explanation.

Q. So -- so at least the hypertension overrode other risk factors including smoking if -- if what you're hypothesizing was the case?

A. In that specific group of patients at that

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specific point in time when they had a heart attack.

Q. Right.

A. Hypertension or hypertrophy, thickness of the heart. You know, the major risk factor for sudden death is -- again from the Framingham study is the degree of hypertrophy that the heart has, thickening of the heart. Hypertension is a powerful cause of hypertrophy of the heart. So, in terms of adverse prognosis, if that relates mainly to death, as it probably did, then that may be another factor, but, you know, I wouldn't -- I -- I certainly wouldn't conclude that smoking was in -- irrelevant to their development of a heart attack.

Q. I -- I was just trying -- I wasn't proposing that, Doctor. I was just asking whether --

A. About their course post-infarction.

Q. A -- yes, and a -- and a different effect in the white people than in the black people from smoking and that perhaps smoking had a -- a lower effect, a lesser effect, in the blacks.

A. Well, from the facts that you stated to me, which I would have to check in that paper which is ten years ago, to be sure about them too, that might

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be one implication, but as a critical reviewer of it, I would raise the issues that I have.

Q. All right. Is hypertension more common in black people --

A. Yes.

Q. -- than white people?

A. Yes.

Q. Are there other risk factors that are more common in black people?

A. It's the main one, but almost certainly, there are other risk factors that are more common. And they tend to be as a generalization not as affluent, not as well educated, involved in manual labor activities to have the higher incidence of blood pressure and at least some of them to be on different diets than the affluent, well-educated people. So, what other -- and there would be the potential of a genetic factor too that is related to race. So, you know, those would be some of the things that would be different.

Q. Is -- is the diet that black people have -- at least I know that diets change, they're different among a lot of people, but again, speaking just generally, is their diet more risky for heart

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disease than the diet of most white people?

A. In the sense that it's not as regulated toward low cholesterol, low fat, low caloric, yes.

Q. All right.

A. And -- and from a different perspective of consuming red meat, it probably isn't. So, they're eating different things and we have to balance -- I'm struggling with the answer.

Q. Okay.

A. We have to balance the risk of red meat consumption versus a diet with not much dedication to being low in cholesterol or low in salt. I think the latter diet would be more risky than one that ate red meat more frequently than it should.

Q. You mentioned hypertrophy of the heart. Is that more common in African-Americans?

A. I believe that it is because of the high risk of hypertension.

Q. I've -- I've seen a reference not to hypertrophy in general, but to left ventricular hypertrophy.

A. That's what -- that's what I'm referring to. It's left ventricular hypertrophy.

Q. All right. And that is a risk factor for heart disease?

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A. It's a risk factor for sudden death and it's a risk factor for heart failure. It's a risk factor for those two.

Q. All right. Is it a risk --

A. It's not a known risk factor for coronary disease development, but in one with coronary disease, it has a very disadvantageous effect by restricting the dilatation of arteries and by requiring more oxygen in the heart than the coronary arteries are able to deliver. Some of my answers are awfully long and --

Q. You said --

A. -- complex.

Q. -- you thought left ventricular hypertrophy was primarily a risk factor for sudden death and for --

A. Heart failure.

Q. For heart failure?

A. But it's very disadvantageous in one who does have coronary disease.

Q. All right.

A. I know of no evidence, believable evidence, that it predisposes to coronary disease, but if you have coronary disease, to have hypertrophy too is unwanted.

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Q. And what would that lead to? What -- what is the effect of that?

A. Well, first you have a much larger muscle mass than you have concomitant change in coronary blood flow. So, in effect, you have a bigger house than you can put furniture into. Is the analogy --

Q. All right.

A. -- apparent? The heart outstrips the blood vessel development, and so it's much harder for me to supply this markedly increased muscle mass with oxygen by blood flow. Second, the hypertrophied heart limits the ability of the coronary artery to vasodilate. If I get ready to run or fight or I'm excited or after a big meal or I exercise, my coronary arteries normally dilate to deliver more oxygen to the heart. In the hypertrophied heart, they cannot do that. It's limited. So, they have an increase in mass, a relative inability to supply that increase in mass with oxygen, both because the development of the coronary arteries does not change in proportion to the development in the mass of the heart and the ability to dilate, to enlarge and supply more flow, is markedly limited in the

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hypertrophied heart. So, these are disadvantageous things once one acquires coronary disease.

Q. All right. What will that lead to in the individual, further disease?

A. It might lead to more frequent heart attacks in one with coronary disease. In one with or without coronary disease, it leads to more heart failure; that is, symptoms of shortness of breath, tiring easily, being unable to work, awakening at night very short of breath, sudden death, organ dysfunction, failure of the kidneys, liver, underperfusion of the brain. These are all consequences of severe heart failure.

Q. When a cardiologist uses heart failure, I -- I suspect, from what you just said, it's not what a lay person might think. I -- I, for example, think if you have an organ that fails, that's it. You're dead.

A. No.

Q. Okay.

A. It's a -- it's an inadequate function of the heart so that one starts to develop consequences of a reduced blood flow to various organs, brain, kidney, liver, skeletal muscle, causing many of

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the symptomatic things that occur. Now, as heart failure progresses, it becomes very, very severe and one develops a -- a totally insufficient delivery of blood and nutrients to these various organs and one dies from it. And one dies in the midst of being very, very short of breath and so on. If you have enough heart failure, you can die suddenly, if you have enough injury to the heart. If you have a huge heart attack and lose a lot of functioning heart muscle, you are in heart failure and you die in shock. You have a major infection of the heart, you can die with heart failure and shock. So, if it's severe enough, what you envision is right, but, generally, it's a progressive kind of thing with increasing symptoms, the kinds I talked about, and evidence to the doctor of progressive failure of the kidneys, failure of the liver related to an inadequate blood flow.

Q. Okay. Are there differences between Hispanics and the rest of the population in terms of the prevalence of various risk factors?

A. Yeah. I -- they have a higher incidence of diabetes. They have a greater incidence of lipid abnormalities. Those two things, I'm certain. I

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would imagine that they probably smoke a little more frequently. I'm not certain of that, but that -- I think that is probably the case.

Q. What do you base that on?

A. Afro-Americans. Just personal experience with patients from all races. My guess would be it's a little higher.

Q. Okay.

A. I may be wrong. Leave it off, if you want. That's just a guess.

Q. It's up to you, Doctor. So --

A. All right. If you want things I'm sure of, diabetes and lipid abnormalities.

Q. All right. How about the typical Hispanic diet in -- among Texas Hispanics?

A. Very high in cholesterol. In fact, do you like Mexican food? You know anything about Mexican food?

Q. Yeah. I love Mexican food.

A. Well, then, you know the answer to the question you asked me.

Q. But I eat it in St. Louis. It may not be --

A. It's probably not too different, although it's a little different.

Q. It's probably not as authentic anyway.

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A. It's very high in cholesterol, in fact. A lot of the Latin-American women are pretty heavy. A lot of the Afro-American women are pretty heavy.

Q. Within Texas?

A. Yeah, within anywhere, but certainly within Texas. I guess that's the other thing I would add. I think the incidence of obesity is higher certainly in Latin-American and Afro-American women than it generally is in Caucasian women.

Q. And -- and you're talking about within Texas?

A. I'm talking about throughout the country, but I would not exclude Texas. I mean in Texas, yeah, and Mexico too. Leave off the smoking business in the Latin-Americans. I might not be right.

Q. When you use the term "Latin-Americans," do you mean the --

A. Hispanic.

Q. -- Hispanics within Texas?

All right. When you have spoken to your patients about the various risk -- risk factors, for example, about smoking and told them that they should -- that they should stop smoking, do you get any argument from them saying, "I don't think it's hurting me"?

A. No. I -- you know, I may never have heard a

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comment like that. And in most instances, there's an acknowledgment that they should.

Q. They knew that already?

A. Uh-huh.

Q. Is there any -- is there any -- just so the record's clear, that was a "yes"?

A. That was "yes."

Q. Okay. Are you aware of anybody in the last 20, 25 years, who has said they thought smoking was not harmful to the cardiovascular system?

A. I have not had a patient tell me that.

Q. All right. Not just restricting it to patients. I just -- I mean anybody.

A. Well, I haven't gone out and sampled a worldwide opinion, so I -- that's not a question I should try to answer. But among the patients that I care for whom I try to get them to stop smoking, there is a general realization that they should. The problem is whether they can or not.

Q. All right. We -- we have just about two or three minutes left on the tape.

A. I'm not too sad to hear that.

Q. So, as I said at the beginning, we had three tapes a day, so thank you very much, Doctor. If --

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MR. CORNFELD: We can go off the record.

THE VIDEOGRAPHER: The time is approximately 6:18 p.m. We're off the record.

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DEPOSITION OF JAMES T. WILLERSON, M.D.

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SIGNATURE OF WITNESS

I have read the foregoing transcript of my deposition taken on the 7th day of September, 1997; and it is a true and accurate record of my testimony given at that time and place, except as to any corrections I have listed on Page 253.

_____
JAMES T. WILLERSON, M.D.

THE STATE OF TEXAS *
COUNTY OF HARRIS *

SUBSCRIBED AND SWORN TO BEFORE ME, the undersigned authority, on this ____ day of _____, 1997.

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